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THE MEDICAL CLINICS
OF
NORTH AMERICA

Volume 13 No 5

CLINIC OF DRS CHARLES SPENCER WILLIAMSON AND CARROLL L BIRCH

RESEARCH AND EDUCATIONAL HOSPITAL, UNIVERSITY OF ILLINOIS

THE MISTAKES IN DIAGNOSIS AS REVEALED BY AUTOPSY

(An Analysis of the Wrong Diagnoses in Four Years of a Medical Service as Revealed by Autopsy)

WE are planning to present to you today a clinic a little out of the ordinary We are not going to show you any cases at all Our clinic will consist of an analysis of a small series of interesting cases who have died and been autopsied

Perhaps I ought to tell you what this is all about Our hospital, as you know, opened April 1, 1925 Last spring we decided that it would be a very desirable thing if we took all the cases who had died on the medical service and been autopsied and compared the clinical findings with the anatomical diagnoses The result showed that we had a total of 170 deaths with 136 postmortems, an average of exactly 80 per cent I may say that we congratulate ourselves on this very high proportion of postmortems because it is far ahead of the average of institutions Every case coming to autopsy has been taken, excepting 4 where the anatomical records were missing, and 4 in which the clinical records were not available We have then, actually 128 cases net, and of these we found that 3 cases had been wrongly diagnosed, 5 cases had been diagnosed in a way which we have called partly wrong, and in one we failed entirely

to make a diagnosis The remaining 119 were substantially correct We shall refer a little later to our criteria of what constitutes a substantially correct diagnosis

For our clinic today we propose to analyze the 9 cases just referred to as entirely wrong, partly wrong, or undiagnosed, and to endeavor to see why we made these erroneous diagnoses

Case I —(We are taking them up in their chronologic order) A brief synopsis of this patient's history is as follows

White male, aged forty-three, entered the hospital May 14, 1926 complaining of nosebleed, bleeding from the gums, black stools, weakness, severe headaches, vomiting of blood, dizziness, and failing vision with bluish-black spots over the entire body The duration of the symptoms had been about four weeks and they were becoming progressively and rather rapidly worse. I may note that this patient was made the subject of a clinic and for the extended details of the case we refer to an earlier number of this publication [1]

The patient further stated that four weeks ago his nose began to bleed without any apparent cause, continuing for four or five hours and stopping spontaneously The next day it started again and kept up until he was nearly exsanguinated and stopped only when the nose had been packed by a physician The next symptom was the appearance of a large number of cutaneous hemorrhages The gums bled freely, at the same time he was vomiting blood and passing it from the bowel But it should be noted that at no time did he have an unusual soreness about the buccal cavity During the last two weeks his vision had been failing steadily

The personal history shows nothing of consequence excepting that in his younger days he had been a hard drinker

Physical Examination —A summary shows that the nostrils, mouth, and teeth were covered with dry blood and the left nostril was still bleeding Otherwise, the head and neck showed nothing abnormal except the pallor There was no sponginess of the gum The neck and chest were normal, except for a few moist râles over the lung and a soft, blowing murmur of the apex of the heart The abdomen was slightly distended and the skin showed many purpuric spots The liver was palpable three fingers below the costal border, regular, firm, not tender, but slightly rounded The spleen was palpable three fingers below the costal border, somewhat softer than the liver, the notch being easily palpated No evidence of ascites The extremities and reflexes were normal

In regard to the diagnosis the following were considered First, benzol poisoning inasmuch as the man worked in a rubber factory However, we found that he had very little if anything, to do with benzol, his job being to trim the tires mechanically Again, the liver and spleen enlargement ruled out this diagnosis The patient's temperature varied from 101° to 102° F and this brought up the question of the possibility of its being a hemorrhagic form of some acute infection, such as smallpox, meningitis, ulcerative endo-

[1] Medical Clinics of North America, Vol 11, No 1, July, 1927

carditis etc. It was considered that the history, with the findings in the liver and spleen ruled these out and we believed we could narrow the diagnosis down to two conditions onmely acute leukemia and purpura hemorrhagica In both of these diseases fever may be and often is present the spleen is enlarged hemorrhages occur from the various organs and beneath the skin with resultant great weakness and prostration Acute leukemia generally has well-defined mouth symptoms which were absolutely absent in this individual

The next step was a careful study of the blood which was made as soon as he entered the hospital with the following result Erythrocytes 900 000 leukocytes 4350 blood platelets 30 000 and hemoglobin 22 per cent The coagulation time was three minutes The bleeding time taken by the Duke method was over sixty nine minutes that is, the tiny puncture in the ear bled for sixty nine minutes freely and was then stopped by the application of horse serum The differential count of the leukocytes was most interesting

	Per cent
Polymorphonuclears	51
Small lymphocytes	20
Large lymphocytes	15
Transitionals	5
Eosinophils	1
Unidentified	8

As I said when the case was first shown far from lessening our difficulties these blood findings rather tended to increase them. It is nearly impossible to make the diagnosis of acute leukemia during an aleukemic period unless the differential count is very decisive A great deal of time and study was given to these blood smears and the cells noted as unidentified were really almost impossible to classify Some of them were undoubtedly atypical myeloblasts and myelocytes. Almost daily examinations of the blood were made and studied by a number of members of the staff who were especially versed in hematology The consensus of opinion was that for the most part these cells were immature which means of course very little except that there is a very active bone marrow and some of the newly formed cells are being swept into the circulation Almost any severe hemorrhagic condition will show a few such cells if there is any regeneration I have seen this more than once in a severe purpura hemorrhagica Further study of the blood was made and the prothrombin test the fragility test and the coagulation time were all carefully studied The first two were normal the coagulation time thirty minutes the clot not retracting for many hours

A transfusion was given almost immediately on entrance. Subsequent blood examinations showed but little change excepting the rise in the red cells and platelets immediately following the transfusion Blood-cultures were negative The tourniquet test was strongly positive This as you know is looked upon as semi pathognomonic of purpura hemorrhagica.

We considered the case to be one of purpura hemorrhagica and called our surgical colleagues into consultation with a view to removing the spleen which was done a day or two later he having had six transfusions before

hand The patient died on the operating table The microscopic examination of spleen and bone-marrow showed the case to be one of acute aleukemic splenomyelogenous leukemia

Now, let us see how we erred in our diagnosis We were well aware of the fact of aleukemic intervals in leukemia, although they rarely ever last any great length of time A very small number of cases have been recorded in which the aleukemia persisted throughout the disease, and this was probably the case with our patient We debated the atypical character of those cells at great length In the light of the autopsy findings they were probably very atypical myeloblasts and the question arises now as it arose then, would he have been justified in diagnosing the case positively as a leukemia on the basis of this number of such cells? I think there might well be a difference of opinion, since every clinician of experience must have seen severe anemias with a small number of myelocytes and myeloblasts in the peripheral circulation The very great diminution of platelets and the positive tourniquet test spoke decidedly in favor of purpura A negative feature is the absence of all mouth symptoms I have seen a fair number of cases of acute leukemia and this is the first case in which I have missed severe inflammatory changes about the mouth, tonsils, or tongue

The autopsy findings showed no gross changes which we had not predicted, a large spleen, a moderate enlargement of the liver, about 2000 grams The lymph-glands were not enlarged except for a few round the abdominal aorta On the basis of these gross findings the pathologist believed that purpura hemorrhagica was the correct diagnosis and it was not until a histologic study of the organs was made and they were found to be packed with myeloblasts that the diagnosis of acute aleukemic myelosis was made The case was considered to be one of such importance and rarity that Professor Jaffé reported the pathologic findings in the Archives of Pathology[1] at great length I quote from a paragraph of this article

"This aleukemic myelosis offers great diagnostic difficulties and may cause diagnostic pitfalls, because there is nothing to indicate the true nature of the disease during life except microscopic examination of the fluid obtained by puncture of the spleen (Hirschfeld and Ferrata) "

Should we have punctured the spleen? I put the question squarely up to you If you had a man who bled for sixty-nine minutes from an insignificant puncture of the ear and could only stop the hemorrhage by the application of horse serum and if this individual had already a blood-count below a million, would you think it justifiable to carry out a splenic puncture? Our answer was emphatically no, especially since we were about to do a splenectomy anyhow

Even according to our present knowledge, I can think of only one thing which we did not do, that is to properly evaluate the very moderate enlargement of the liver We explained the enlargement of the liver as of alcoholic origin because of his history of excessive drinking This is much more apt to occur in a leukemic condition than in a purpura, and it may be that we should have laid more stress upon this fact I leave you to determine whether or not this is so

[1] Jaffé, R H Arch Path and Lab Med, 1927 (January), iii, 60–72

Case II.—A white male aged sixty eight entered the hospital August 13 1928 at 4 P M He had been treated in the Out Patient Department since July 31 1928 and the diagnosis had been made of an old fibrous healed tuberculosis bronchitis with apparent bronchiectasis (left) and enlarged heart and aorta and it is noted that the x ray findings confirm the physical diagnosis. He was not seen in the Dispensary from July 31st until August 13th when he returned in very bad condition It was late in the afternoon and he was only seen by one of the interns who went over him carefully and wrote a good history He noted the findings in the lung above referred to as

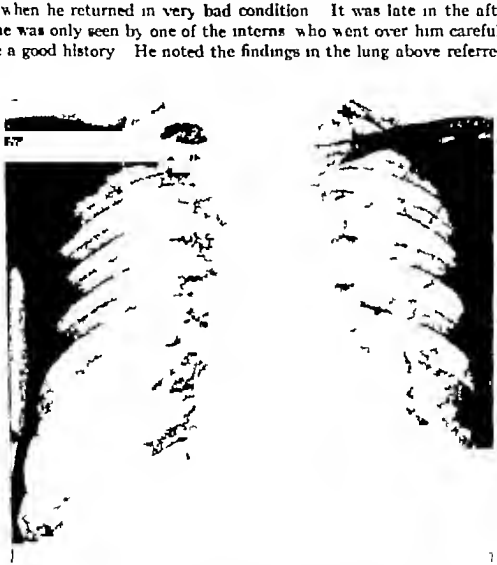

Fig 173.—Print from x ray plate of chest of Case II showing the picture of a bronchiectasis rather than an empyema This plate was taken three weeks before death.

bronchiectasis. The dulness was so marked however that he considered it to be an atelectatic condition The patient was afebrile and was in an almost dying condition so that it was quite impossible to repeat the x ray which had been taken three weeks previously The blood-count was only 10 800 leukocytes 3 800 000 red cells and 58 per cent hemoglobin The patient died the following night before any of the attending staff had seen him he having been in the hospital only about thirty hours It seems quite evident that the intern considered that the dulness over the left lung posteriorly was an atelectasis and this it seems to me was the most natural conclusion since

the patient had no fever and but slight increase in the leukocyte count I am not able to say whether he had intended to make an exploratory aspiration, but I doubt if he did because of the patient's desperate condition

The autopsy findings revealed an encysted empyema, with 600 c c of thick pus The other findings were inconsequential The accompanying x-ray (Fig 173) shows, I think you will agree, rather the picture of a bronchiectasis than that of an empyema, encysted or otherwise, but it will be remembered that this x ray was taken three weeks previously and the patient was admitted in a dying condition, so another one could not be taken It seems to me that the explanation is probably this, that the empyema was secondary to an old bronchiectasis, at least no other explanation was found at autopsy A more experienced clinician might have risked a diagnostic puncture in spite of the desperate condition of the patient

Case III —This is a white female, aged seventy-six, who entered the hospital July 13, 1928 It is one of the most interesting cases it has been my fortune to see in a long time The patient complained of (1) pain in the small of her back which had existed for four or five years, (2) loss of weight amounting to 40 pounds in the last year, (3) distention of the abdomen, which had been present for four months, with nausea, vomiting, and loss of appetite

Onset and Course —The patient stated that previous to four months ago she had been in good health except for pain in the small of her back These pains would start on the right side of the sacrum and flash across the pelvis It was a sticking, momentary pain, but very severe Four months ago she went to another hospital to have her back x-rayed and while there they made a pyelogram which, she states, caused her to suffer a great deal, and to this she attributes her present distress She says that since then she has had no appetite, often going for two days without food She is tired and weak all of the time, but has not been confined to bed About this time she began having distention and a sense of fulness after eating She does not belch and has no difficulty getting her breath and has no abdominal pain The back pain has persisted and is present whenever she lies down

She states that she has lost 40 pounds in the last year or year and a half The first loss was noticed shortly after having some teeth extracted

Under the caption of general and negative, we find nothing which throws any light upon her condition except that she has been constipated for a few months Likewise, the family and pathologic history is quite negative

Physical Examination —A very old and poorly nourished white female, feeble and apparently anemic Head, neck, and chest were substantially negative, with the exception of a soft blowing apical systolic murmur which was interpreted as anemic

A most careful examination of the abdomen showed no palpable masses, no enlargement of the liver, spleen, or kidney and no tenderness or rigidity

The back showed a slight general kyphosis, but no areas of tenderness The extremities were negative, no adenopathy or edema The reflexes were all present and normal

The patient had a temperature of 100 5° F on entrance, which dropped to approximately normal the next day, but then went up again and remained

above normal throughout the entire course of disease averaging perhaps 101° F but very irregular

The intern's preliminary diagnosis was malignancy probably of the stomach

The blood examination showed 3 300 000 red cells 50 per cent hemoglobin 10 900 white cells Urinalysis showed a trace of albumin and a moderate number of pus-cells in an uncatheterized specimen An Ewald test breakfast was given removed at one hour when 113 c.c. were recovered There was a complete absence of free acid and a total acidity of 6 degrees no occult blood Microscopically many cocci and a few bacilli were found the latter however not having the characteristics of the Oppler Boas bacillus Several examinations of the stool were made three to be exact and in each of these occult blood was found in small amounts Chemical findings of this sort lent I am sure you will agree additional evidence to the tentative diagnosis of carcinoma of the stomach The patient was then sent down for a gastro-intestinal x ray study with a clinical diagnosis of possible malignancy of the stomach I quote the x ray report

'The preliminary fluoroscopic examination of the chest showed tortuosity of the aorta indicative of an arteriosclerosis Examination of the stomach and duodenum with an opaque meal showed an irregular filling defect in the pyloric end of the stomach No interference with evacuation no six hour residue Roentgen diagnosis Probable carcinoma pyloric end of the stomach (Fig 174)

We were unable to see then and we are unable to see now any symptom or sign which would call in question the diagnosis of carcinoma of the stomach Because of her age and feebleness we did not repeat the test breakfast After being in the hospital her liver increased steadily in size and became plainly palpable which we attributed to the development of liver metastases I have already stated the patient was running some degree of fever We noted this and explained it by the rapid development of the liver metastases In other clinics I have discussed this matter at some length as it is not very infrequent Von Frerichs in his monograph on liver diseases, called particular attention to it and I have seen more than one case of much higher fever than this where the autopsy showed large numbers of liver metastases Why it develops in some cases and not in others is not clear At no time in the history of the case were any glands palpable especially no glands near the clavicle which are so commonly looked upon as an early diagnostic finding of carcinoma of the stomach Neither did the x ray show any enlargement of the tracheobronchial glands

Autopsy Findings.—When the abdomen was opened the liver was seen to be full of metastases evidently malignant and the pathologist remarked that the diagnosis was evidently quite correct When it came to the stomach however this organ was found to be entirely normal What had mimicked the picture of a gastric tumor was a mass of markedly enlarged retroperitoneal glands, pushing forward and making definite pressure on the stomach All the other organs were practically normal There were a few metastases in the spleen The pancreas uterus and other common sources of carcinoma were all negative

It was not until the histologic report was completed that the diagnosis could be made, and then to our great surprise it was found that the retroperitoneal lymph-nodes gave the classical histologic picture of Hodgkin's disease The same is true of the metastases in the liver and the spleen

Where lay our mistake? Much pondering over this leaves me free to say that I think I would make the same diagnosis again tomorrow under the same premises While fever is by no means a regular feature of carcinoma, it certainly is much commoner in this disease than is the existence of a Hodgkin's disease limited to a few retroperitoneal glands, with metastases in the

Fig 174 —Print from x-ray plate of stomach and duodenum of Case III Note the irregular filling defect in the pyloric end of the stomach

liver and spleen On the other hand, fever is not constant in Hodgkin's disease I really think that a correct diagnosis in this case was simply "not on the cards"

You will see in the appended x ray (Fig 174) the justification for the roentgenologic diagnosis of carcinoma of the stomach Just why she should have had an achylia is not clear

The above three cases we have classified as frankly wrong diagnoses Another very interesting case we had to leave undiagnosed

Case IV.—A white female aged twenty nine came into the hospital April 10 1929 and died April 13th The patient was married and had a baby fifteen days old.

Complaints.—Abdominal cramps and diarrhea these two having lasted about nine weeks in addition loss of weight and fever which she insisted she had had for nine months. The patient was well until her last pregnancy During the first few weeks of her pregnancy she had severe nausea and vomiting and ran a daily temperature from 99 to 100 F At the end of four months period her vomiting ceased and the patient felt very well although she continued to lose weight Later in the pregnancy the vomiting started again the exact time she does not know Nine weeks ago she began to have severe cramp-like abdominal pains accompanied by a severe diarrhea. The stools were yellow in color and watery in consistency There had never been either blood or mucus in the stools until the day of admission to the hospital when streaks of dark blood were seen She had been confined to bed for two months under the care of her family physician but in spite of appropriate treatment the diarrhea and abdominal pain have persisted Fifteen days ago she gave birth to a male child weighing 4 pounds 10 ounces delivered spontaneously after a three-day labor There was no postpartum hemorrhage or other complications known to the patient or her family Since her delivery her temperature has risen daily to 104° F in the late afternoon falling to 101° F in the morning The abdominal pain persisted until two days ago when it was very severe but since then has ceased She has noted very great distention of the abdomen since her delivery Four months ago she weighed 104 pounds at present she weighs 95 pounds

If we ignored the history a temperature of 103 or 104° F shortly after a delivery under circumstances unknown to us would suggest some septic pelvic complications and we went at the case from this angle However we found the pelvic examination negative and a blood-count to our surprise showed less than 3000 leukocytes with 71 per cent. polymorphonuclears 27 per cent. lymphocytes The red count was a little over 4 000 000 with 67 per cent hemoglobin The urine showed a small amount of albumin with a moderate number of pus-cells and a few blood-cells.

Having ruled out we thought septic complications in view of the very low blood-count and high fever we thought of malaria, typhoid and tuberculosis. The patient had been visiting in Tennessee so that the two former diseases were not improbable Careful examinations of the blood showed no parasites and the blood-culture was negative as was also the Widal test for bacillus typhosus para A and para B Stool examinations for parasites were negative. The patient had however several stools in the hospital containing large quantities of blood

On the 12th it was noted that the abdomen was greatly distended the spleen about three times normal size and plainly palpable. The stools consisted almost entirely of blood The lungs showed a diffuse bronchitis The Wassermann was negative. As the patient had no cough no sputum was obtainable for examination

While the patient looked seriously ill her condition was not considered at all critical This last report was written Friday afternoon and the in

tern expected that the case would be gone over again carefully on Monday as usual To the great surprise of everybody at 3 o'clock Saturday afternoon she suddenly expired, having previously passed a large amount of blood from the bowel The death was clearly from hemorrhage No formal diagnosis had been made Of course, it was clear that some ulcerative condition existed in the bowel The autopsy was made almost at once and the condition found to be a generalized tuberculosis with the lungs full of miliary tubercles and deep, old ulcerations in the bowel, especially about the cecum It was from one of these ulcers that the fatal and unexpected hemorrhage occurred

Why was the diagnosis not made? Primarily, I think we can say because of the short time in hospital and the very unexpected sudden death We had attempted to have a chest plate made with a portable apparatus but the patient was so sick and uncoöperative that it was not successful None of the attending staff saw the case after Friday afternoon, at which time the reports of the blood-culture and Widal had not returned and you will note they did not come in, as a matter of fact, until the patient was dead I think we were correct in first ruling out septic conditions, then malaria, then typhoid, and I feel sure that had she lived until Monday the diagnosis would have been correctly made However, we have chalked it up as a missed diagnosis

PARTLY WRONG DIAGNOSES

Case V —This was a white male, aged sixty-six, who came into the hospital in a very weak condition, unable to walk without assistance

Complaints —His complaints were pain in the back, dizziness, cough, loss of weight, weakness, involuntary bowel movements, all of these symptoms dating back three or four weeks He stated that he had become very dizzy and fainted while at work He was taken home in a cab and had been in bed ever since He has had intermittent cough for several weeks which is loose and has not bothered him much He has become so weak that he can scarcely move his legs The involuntary bowel movements had existed for many years following hemorrhoidectomy

Past History —He has had a great deal of trouble with his teeth and with his heart, especially about a year ago Since then he seems "to go to pieces" on slight exertion He has had shortness of breath for a long time

The symptoms as you see, were indefinite His personal history was quite negative, and the physical examination showed only a moderate enlargement of the heart, with very distant tones, hardly audible The abdomen showed a good deal of tenderness, the liver being palpable just below the costal margin, with a sharp edge and some tenderness over it The spleen was not enlarged A notation on May 29th states that there was a definite consolidation in the right lower lobe posteriorly, with many fine moist râles At this time a diagnosis of bronchopneumonia was made

The blood examination showed 4,600,000 red cells, 11,000 white cells, with 62 per cent polymorphonuclears The patient had a moderate temperature on entrance and at the end of the second day it rose to 105° F , the next day to 106° F , coming down to normal in the morning Careful examina-

tions were made for malarial parasites and none found A blood-culture was made and a small bacillus Gram negative was isolated from the blood The Widal was negative. The laboratory could not identify the organism which had been cultured from the blood.

As the case then stood the patient had an evident bronchopneumonia a severe myocardial degeneration due to an unknown organism which had been recovered from the blood and which the laboratory did not believe to be typhoid The patient died suddenly and rather unexpectedly on June 4 1925 after having been in the hospital twelve days Our feeling was that the severe septicemia was due to typhoid but in the absence of a positive Widal and the assurance of the laboratory that the organism was not the typhoid bacillus we made no diagnosis at all and signed him out as a bronchopneumonia and myocarditis. The autopsy disclosed frank typhoid One very odd fact disclosed at autopsy was that the spleen was not enlarged and the liver was considerably so probably due to venous congestion This was in exact accordance with our clinical findings

How could we have diagnosed the typhoid end of it? Having thought of typhoid having made a blood-culture with this definitely in mind and having received a laboratory assurance that it was not typhoid and the Widal being negative I think we shall have to say that we just lacked the courage to insist that it was typhoid in spite of the fact that they could not identify the organism which had been cultured It is interesting to note that after the autopsy was made and the diagnosis of typhoid established the blood-culture came back marked positive which however did not help us very much Someone has asked the question What would have been the diagnosis in the days before blood-cultures were done? I think undoubtedly typhoid with bronchopneumonia and myocarditis Laboratory work is of the greatest service when faultlessly done as is the x ray but when poorly done it often leads to mistaken diagnosis

Case VI.—A white male aged thirty five entered the hospital January 25 1926 and died February 23 1926 This patient may be very briefly summarized. He was an old dispensary patient who was finally admitted to the hospital because of extreme dyspnea and great pain particularly in the abdomen He had marked enlargement of the thyroid gland of all the cervical glands and as shown by a chest plate (Fig 175) of all the mediastinal glands. The axillary and inguinal glands were also moderately enlarged He ran an irregular temperature and a Hodgkin s was first thought of Our diagnosis was mediastinal tumor probably Hodgkin s disease One of the glands in the neck was removed for a biopsy The report of the biopsy was malignant tumor probably carcinomatous degeneration of a retrosternal goiter In view of this biopsy report we changed our diagnosis to carcinoma of the thyroid The patient died shortly after and the autopsy report is as follows

Thymoma (malignant tumor of the thymus) with metastases in the cervical and abdominal lymph glands bronchopneumonia etc. I am tempted to say as I did in the last case that in many cases laboratory work is very helpful and in others when incorrect it leads to an incorrect diagnosis as it

did in this case It is only fair to say, however, that if we had not had the biopsy we should have made another but equally incorrect diagnosis

Fig 175 —Print from x-ray plate of chest of Case VI showing massive enlargement of mediastinal glands The shadow of the enlarged thyroid is also evident

Case VII —A male, aged forty-four, entered the hospital January 10, 1928 and died January 18, 1928 The salient points in this case may also be quite briefly summarized The patient had been in the hospital previously and had been discharged with a diagnosis of hypernephroma with metastases in the lung

Physical Findings —The summary of these showed that the right eyeball was slightly protruding and that the pupil was larger than on the left side The chest showed a projecting mass at the upper part of the sternum at its left edge, about 9 × 11 cm., projecting ½ cm from the surface It was firm, not fluctuating and not pulsating, and was very tender to pressure The lungs showed fine moist râles all over, particularly over the left base which was also dull and with increased tactile fremitus Heart was substantially negative The liver was 1½ cm below the costal border, the spleen not palpable The left kidney was large, irregular, about 4 cm below the costal margin and tender The left testicle had been removed, and the patient

stated that the operation had been performed for a 'ruptured testicle' which he was told had turned into a tumor It was quite evident that the individual had a large number of metastases in the sternum as shown by the physical examination and in the lungs as shown by the x rays (Fig 176) The only question at issue was whether the tumor in the left kidney was a primary hypernephroma or whether it was a metastasis and the primary tumor was in the testicle which had been removed Both of these were thought of and discussed and both are recorded in the history with the testicular tumor diag

Fig 176—Print from x ray plate of chest of Case VII showing metastases in lungs.

nosis first However later questioning seemed to throw considerable doubt on the tumor of the testicle. He had been injured and stated that his testicle was ruptured and this led us away from the correct diagnosis. The urinary findings were entirely consistent with the hypernephroma, and the lung metastases fitted in perfectly with this assumption Indeed you may remember a case we recently showed where the lung metastases were recognized before the primary hypernephroma

The autopsy diagnosis is as follows

Metastases of a fibrosarcoma to the lungs to both kidneys especially

the left, to the liver and the spleen Local recurrence in the left scrotum Primary tumor probably in left testicle "

Case VIII —Patient is a white male, aged forty-two, who entered the hospital February 23, 1929 and died March 4th

Present Complaint —Pain in the back, weakness, and loss of weight amounting to 30 pounds in four months, pain in the left thorax for three weeks He felt well until four months ago when he contracted a cold, from which he recovered, but which was followed by arthritic pain in the back He developed progressive weakness, then caught another cold three weeks ago, with associated pain in the left chest

General and Negative —Dyspnea on exertion and heart consciousness

His past history was negative except for rheumatism at eighteen

Physical examination was substantially negative Blood-pressure was 104/46 The laboratory findings showed a urine containing large amounts of albumen, with casts and blood The patient's condition was subfebrile, much of the time subnormal, the highest temperature recorded was 100° F The blood examination showed 2,800,000 red cells, 8200 white cells, with 81 per cent polymorphonuclears and a hemoglobin of 38 per cent The phenosulphonephthalein injected intravenously showed only 5 per cent output in three hours The blood chemistry showed an NPN of 200 mg and blood-sugar 125, creatinin 5 46 per 100 c c of whole blood An *x*-ray was made of the lungs and kidneys with negative results The Wassermann was negative Examination of the eye grounds was negative The blood culture was positive, showing a long chain Streptococcus viridans This latter finding fitted in perfectly with the clinical diagnosis and so the patient was signed out as a subacute bacterial endocarditis This part of the diagnosis was also shown by the autopsy to be correct Just before he died, however, he developed a marked cyanosis, his breathing became deep and at times of the Cheyne Stokes variety, and the blood-pressure rose to 216 systolic A vene section was made, but the patient died the same day There was no evidence of paralysis obtainable The autopsy showed that in addition to the bacterial endocarditis which we had diagnosed, the patient had a hemorrhage in the brain which we had not diagnosed and which was apparently the immediate cause of death A large hemorrhage had occurred in the occipital gyrus and ruptured through into the ventricles and through the isthmus into the fourth ventricle I neglected to say that we had also made the diagnosis, which was quite evident, of a chronic glomerular nephritis, which was substantiated at autopsy

Now the question is, Could we and should we have diagnosed the cerebral hemorrhage? Under those circumstances, with the extraordinarily high blood-pressure and an active septic process, a hemorrhage was quite possible, indeed even probable On the other hand, the patient had almost no phthalein output and was ripe to go into uremia at any moment If the hemorrhage had been one of the usual types in the internal capsule, so that it made a hemiplegia, the diagnosis would have been simple enough With a tremendous burst of blood into the ventricles and death shortly after, I question if anyone could have made the diagnosis At any rate, we did not

Case IX.—This is a white male aged sixty, who entered the hospital May 13 1929 and died May 21

Present Complaint—Enlarged liver pain in upper right quadrant heartburn nausea belching, with some minor complaints

Onset and Course—He states that the pain in the right upper quadrant began about six months ago It was a dull ache and quite constant. At that time he saw a physician who told him that his liver was enlarged For fifteen years he had complained of heartburn About once a week he had nausea, without vomiting however This occurred only when his stomach was empty After nearly every meal he had belching During the past eight months he discovered that his heart skipped beats and three years ago his physician told him he had endocarditis and myocarditis He had been taking digitalis since 1925 He complained of pain in the kidney region generally dull but at times severe.

He had lost 45 pounds in weight in four months The remainder of the history is unimportant.

Physical Examination—This was substantially negative except for examination of the abdomen The liver was 4 inches below the costal margin nodular rough and tender A mass the size of a hen's egg or a small fist, was palpable in the left upper quadrant The entire abdomen was tender and a little fluid was present

There was some edema of the legs and feet The urine showed a little albumen and a few blood-corpuscles The blood-count showed leukocytes 11 000 with 83 per cent. polymorphonuclears, 90 per cent hemoglobin and 6 000 000 erythrocytes. This we attributed to a concentration of the blood The gastric contents showed an achylia. This was one of the first cases in which we used the neutral red test. We found the dye appeared in forty five minutes and free hydrochloric acid 8 degrees in forty five minutes with a total acidity of 18 In other words the findings were such as would indicate an achlorhydria but not a true achylia. This fitted in with our conception of the case

The patient was then sent down for a gastro-intestinal series with a tentative diagnosis of carcinoma of the stomach The report reads as follows

Re-examination of the stomach and duodenum with opaque meal showed the same findings noted on previous examinations There was irregular narrowing of the pyloric end of the stomach suggestive of pressure from without rather than due to intragastric lesion However the possibility of a carcinoma involving the pyloric end of the stomach could not be definitely excluded (Fig 17*1*)

Patient died shortly after

Autopsy Report—The salient features of this were an enormous liver over 4000 grams with many metastases The stomach was normal. What had simulated a carcinoma of the stomach was a mass of enormous glands retroperitoneal with the primary tumor in the sigmoid at the junction of the iliac and pelvic colon

Why did we not recognize the lesion in the colon? I think we should have done so I think we were so well satisfied with the diagnosis of carcinoma of the stomach with metastases in the liver that we overlooked the fact as

suggested in the x-ray report, that this also could be due to pressure from without Now, of course, a colon tumor is anatomically incapable of making pressure on the stomach, but metastatic glands may, and actually did, do so I think we should have made use of the barium enema which might have shed more light on the subject On the other hand, granting that this had been

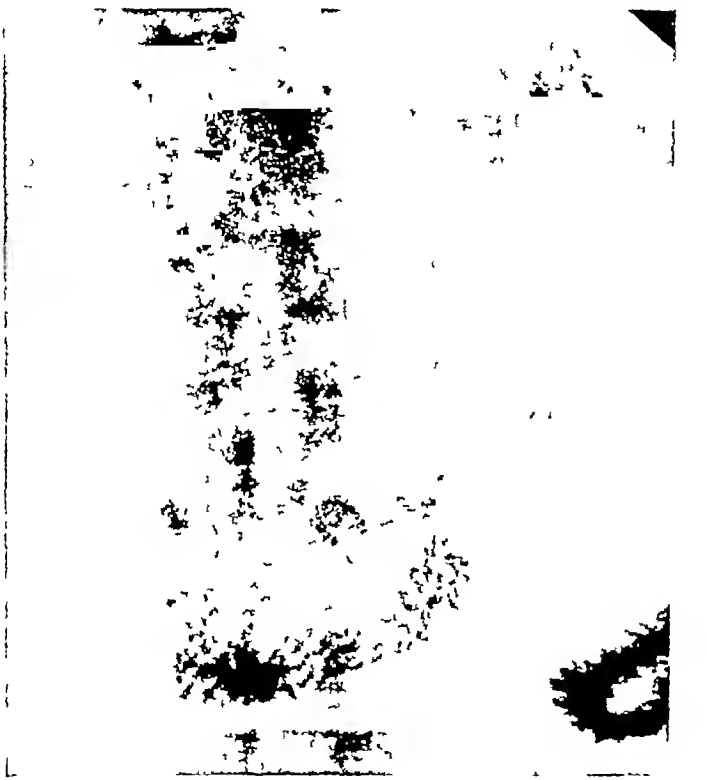

Fig 177 —Print from x-ray plate of stomach and duodenum of Case IX There is irregular narrowing of the pyloric end of the stomach suggestive of pressure from without rather than an intragastric lesion However, the possibility of a carcinoma involving the pyloric end of the stomach could not be definitely excluded

done, and that we had found a constriction of the sigmoid, we would have been in the same predicament that we were with the stomach, namely, that this might have been due to pressure from the outside In any event, we should have made the colon examination

With this case we bring to an end the list of those which we have regarded as wrong or partly wrong The rest of the series we have called substantially correct It is extraordinarily

difficult to frame a definition of what constitutes a substantially correct diagnosis, so I am going to take the liberty of just briefly giving a number of examples

To begin with, a substantially correct diagnosis must be one that adequately explains the cause of death with an understanding of the more important contributing causes

Terminal conditions, such as small infarcts in the lung, hypostatic pneumonias, multiple gastric erosions, hydrothorax, and other evidences of stasis which occur quite regularly in the course of all diseases due to cardiac failure, we consider as part and parcel of the mode of death, and exclude them from our consideration The following may serve as examples of what we call substantially correct diagnoses

A patient had pernicious anemia and gall stones and both of these conditions were substantiated at autopsy In addition she had a narrowing of the bowel due to an old tuberculosis This latter had no bearing upon the symptoms and was in no way associated with her death.

A man, who had been diagnosed as portal cirrhosis and had been tapped many times in the course of an eighteen months' observation, was found at autopsy to have a typical portal cirrhosis which was the cause of death In addition, he had a small carcinoma of the splenic flexure of the colon with no metastases We regard the latter as an accidental finding

A middle aged man died of luetic aortitis and myocarditis, with resultant cardiac decompensation The autopsy confirmed these findings fully, but in addition found a very small aneurysmal sac, 3 cm in diameter, at the root of the aorta The *x*-ray examination had been entirely negative and since the symptoms were in no wise due to the aneurysm, and since it in no wise contributed to his death, we regard it as an accidental finding

A patient who died of gangrene of the leg associated with an arteriosclerosis was found at autopsy to have these, but in addition showed some acute changes in the mitral valve The patient was sixty nine years of age The cause of death was, in reality, a general sepsis from a gangrene and we regard the

recent changes in the mitral valve as inconsequential and accidental

A man who died of chronic myocarditis with myocardial insufficiency was found at autopsy to have both of these In addition, he had numerous gastric erosions and gall-stones, neither of which had made any symptoms and the former of which were undoubtedly terminal We regard these as accidental findings

A patient dying of erysipelas was found to have an acute myocarditis and a hemorrhagic colitis It was known clinically that she had numerous bloody stools We regard the myocarditis as part and parcel of the mechanism of death In other words, any patient dying from an acute infectious disease such as erysipelas is certain to show a parenchymatous change in all the organs

Our last case was one in which the clinical diagnosis was carcinoma of the pancreas and in which the autopsy report showed carcinoma involving the pancreas and the common bile-duct, and it was believed that the origin was in the common bile-duct The autopsy report states that the head of the pancreas is replaced by a large, stony, hard mass and there was another stony hard mass projecting into the common duct In this case it seems a matter of total indifference and one which is perhaps a matter of opinion as to which was primary, since both were about equally involved

I think we shall close our clinic with a short discussion of a most unusual case He was a white male, aged forty-eight, who entered the hospital February 27, 1929 and died April 3, 1929 Briefly stated, the patient came in with very few subjective symptoms, but with a large number of gland groups greatly enlarged Examination showed that the cervical glands were greatly enlarged, the axillary likewise, the inguinals constituted huge masses on each side, with, however, no enlargement of the intrathoracic glands The inguinal glands showed a matting together of the different masses and an infiltration of the overlying skin The blood findings were normal For these reasons one of us (C S W) showed him in the clinic as a lympho-

sarcoma This diagnosis was made because of the character of the glandular enlargement with negative blood findings and only moderate enlargement of the spleen The inguinal glands were removed and sent to the pathologic department for examination The biopsy report reads as follows

"Generalized, giant, follicular hyperplasia "

The interesting part of the case came just before death I have already stated that the blood findings were negative To be exact, he had 5,650,000 red cells 60 per cent hemoglobin, and 6600 leukocytes, with a differential count of 64 per cent polymorphonuclears, 32 per cent lymphocytes, 3 per cent large mononuclears, 1 per cent monocytes, and 4 per cent transitionals This was confirmed by several subsequent examinations, and the last count, which was made on April 3d, the day of his death, gave 317,000 leukocytes, with about the same differential as before Now came the interesting question, Was this an aleukemic leukemia with a terminal exacerbation, or was it simply a lymphosarcoma or other glandular condition with a terminal leukemic picture, which happens occasionally? On the one hand, we had glands which were coalescent, rapidly growing, with a perfectly normal blood picture, as already stated It is interesting to note that the biopsy report finds just ordinary glandular hyperplasia of a giant follicular type

The autopsy report which I here show you, diagnosed first leukemia, as is shown in typewriting, and then the final diagnosis of lymphosarcoma I am told that the case was so unusual that sections of the glands were sent to a number of pathologists throughout the country and that the diagnosis lymphosarcoma represents a majority, but by no means unanimous, vote Perhaps, in concluding, we can do no better than to state that this is a conspicuous example of how much we have yet to learn both clinically and pathologically of the diseases associated with generalized glandular enlargement

CLINIC OF DR LEWIS J POLLOCK

NORTHWESTERN UNIVERSITY MEDICAL SCHOOL

DISORDERS OF SLEEP

THERE are many disorders which occur during sleep or in some way simulate sleep which must be clearly differentiated from the true disorders of sleep One of the common disorders is predormescent or indormescent start, in which the patient suddenly awakens with a start, at times associated with a dream of falling, or at times as he is falling into sleep he is startled into wakefulness These starts are frequently a potent factor in the production of insomnia and in the genesis of numbers of fears, particularly those dealing with the fear of death Night terrors characterized by recurring attacks of terror from which the patient awakens and for a period of time is disoriented, expressing wildest alarm, screaming, and at times attempting to escape, are frequently encountered in children Often hallucinations occur, and frequently there is a loss of memory for the attack.

Nightmares or terrifying dreams occur at any age They are perhaps only a milder form of night terror They differ usually in an absence of a state of disorientation and amnesia following the terrifying dreams The exciting cause of both conditions may at times be found in peripheral stimuli resulting from partial asphyxiation, as by a poorly ventilated room, having the face covered by blankets, or being too tightly restrained in covers, respiratory difficulty as the result of disease occluding the nasal passages, bronchial asthma, decompensated heart lesions, or labyrinthine stimuli resulting from aural disease and exposure to cold

Somnambulism, as well as some forms of "moon walking,"

although occurring during sleep or, perhaps better stated, interrupting sleep, are the result of mental mechanisms which operate in hysteria They are only accidents occurring during sleep The mental mechanisms involved in night terrors and terrifying dreams may likewise be explained upon the basis of a dissociation of consciousness or a symbolization of a repressed unfulfilled wish, according to the particular philosophy of the psychiatrist

Of the conditions which imitate sleep in some way mention should be made of hysterical sleep, known by various names, as "death trance," "passive somnambulism," and so forth These states resemble sleep only in that the observer is unable to determine any reaction to ordinary external stimuli in the lethargic patient These states may continue for years and are only a symptom of hysteria

Symptomatic narcolepsy, or attacks of sleep, may occur as the result of hysteria where there is only an apparent loss of consciousness, and in epilepsy, in organic disease of the brain, and at times of other parts of the body The type of somnolence occurring in African sleeping sickness or trypanosomiasis has been classified as a narcolepsy by some authors Of the diseases of the brain it occurs fairly often in brain tumor and tuberculous meningitis, and has been described in acute superior polioencephalitis In epilepsy such attacks are often equivalents, and when the patient is awakened he may present a picture of excitement or delirium In these cases the condition does not resemble normal sleep so much as the somnolence which follows an ordinary epileptic convulsion Difficulty in remaining awake is seen in many organic diseases of the body, some associated with pluriglandular disease or dysfunction of some gland of internal secretion, as myxedema and disease of the pituitary gland This is likewise observed in senility, in cardiovascular disease, perhaps related to a cerebral anemia, and in renal and metabolic diseases with intoxication where the somnolence is an early manifestation of an intoxication which may lead to a lethargy, stupor, or coma These states differ from sleep in their gradual appearance, and in the inability to awaken the patient

rapidly Consciousness is never lost in a few moments as in sleep or true narcolepsy Somnolence is characteristically and frequently found in all cases of increased intracranial pressure resulting from brain tumor, particularly with hydrocephalus

It is noteworthy that lesions of the midbrain and cases with secondary hydrocephalus, which are always associated with a distended third ventricle with damage to the hypothalamic region, are predominantly associated with somnolence It has been noted frequently that diseases of the pituitary gland are associated with disturbances of sleep As an example, the following case may be cited

A man aged fifty with no notable antecedent disease developed a polyuria and polydipsia He complained of increased fatigue and rapid diminution of sexual interest and potency Physical examination at this time revealed no abnormality A short time afterward he began to complain of bitemporal headaches which were of a dull aching character at times worse at night. He became easily chilled and at times noted some diminution in visual acuity A rather rapid emaciation followed and at the same time the heretofore existing polyuria disappeared Somnolence developed and within a period of two weeks he entered into a sleep from which he could be aroused but into which he would immediately relapse upon cessation of external stimuli When aroused it was found he had a bitemporal hemianopsia A diagnosis of tumor of the hypophysis was made but the general condition of the patient was such that it was felt he could not survive an operative procedure. Necropsy revealed a rather rare tumor a melanosarcoma of the pituitary gland

This state of somnolence resembles very much the hibernation observed in lower species It is always associated with low blood pressure and marked hypothermia It is interesting to note the co-existence of the disturbance in water balance, and we will see the same existence of polyuria with disturbances of sleep in other diseases

Frequently instead of hibernation we may be confronted with true narcolepsy in which the patient has an irresistable desire to sleep, irrespective of what he may be doing at the time—walking, talking, or engaged in any other activity A patient may fall asleep and remain asleep for a short period of time and awaken quite refreshed There is on record a case of narcolepsy in which a brakeman frequently had such attacks while walking

along the tops of moving trains, without having fallen This case is of great importance from a physiologic standpoint, in that it shows that muscular relaxation is not a necessary accompaniment, or prelude, to at least this type of sleep Not only do these cases of narcolepsy occur in diseases of the pituitary gland, as expressed by tumors or compression, as by a distended third ventricle, and so forth, but they may occur from dysfunction of the gland without known pathology A young man, aged twenty-two, presenting all of the characteristics of Froelich's syndrome, with adiposity and absence of secondary sexual characteristics, presented himself for treatment for frequently recurring attacks of sleep of very short duration The most careful examination revealed no evidence of any pathology about the pituitary gland or in the brain, and he has been observed for a period of fifteen years without the development of any symptoms referable to intracranial disease The condition may at times be seen following skull fracture at the base, as in the following case

A young married woman, while driving an automobile at high speed, ran into another machine at the intersection of two roads She was thrown forward through the windshield and then thrown back against the seat She lost consciousness for three hours When consciousness returned she complained of a severe headache which persisted for about a week, during which time she was restless, excitable, had marked insomnia, and generalized muscular twitchings A bloody spinal fluid was obtained upon spinal puncture, but no evidence of skull fracture or injury to the brain could be elicited She left the hospital at the end of the second week, and only then developed a very pronounced polydipsia, and passed from 7 to 8 quarts of urine daily At the same time she developed an irresistable desire to sleep, and would fall asleep while standing and talking to her friends, sleep from a few minutes to as long as ten, perhaps leaning against a table or a chair, then awakening quite refreshed No other signs of intracranial injury were found

The coincidence of disturbance in water balance with attacks of somnolence leads one to the speculation that it is not the pituitary gland itself which is disturbed in the diseases and injuries producing these conditions It is much more likely that the disturbance of water balance and the disturbance of sleep both are the result of damage to the hypothalamic region from

which the stalk of the pituitary originates This appears to be the more likely because of many observations made upon patients suffering with the sequelæ of epidemic encephalitis or encephalitis lethargica

During the recent epidemic of encephalitis lathargica disturbances of sleep were among the most common symptoms to be observed The most prominent disturbance was that of somnolence or lethargy from which the disease has obtained one of its names In contradistinction to the clouding of consciousness which is the result of intoxication and is a precursor of stupor and coma, this somnolence had many of the characteristics of ordinary sleep The patient could be aroused from sleep by ordinary stimuli, was promptly oriented, and showed no clouding of consciousness As long as he was stimulated he remained awake If then left alone he promptly fell asleep He acted exactly as an individual who had been kept awake a number of hours In this disease the pathology is limited more or less to the basal ganglia, the midbrain, and the hypothalamic region Frequently cerebral adiposity and diabetes insipidus resulted Not only were somnolescent states observed, but many other interesting conditions of disordered sleep occurred At times during the acute illness, but more frequently following it, insomnia occurred This insomnia, in contradistinction to that which is functional in origin, could not be controlled short of anesthetizing the patient It was often associated with some motor disturbance, such as a stereotyped movement of the arm but it is important to note that in other cases motor disturbances of spasticity, tremor, dystonias, etc, commonly following in the wake of this disease were not associated with sleep disturbances Equally significant was the occurrence of sleep reversal, wherein the patient was unable to sleep during the night, but during the day fell asleep promptly and slept peacefully, although not refreshed Attempts to keep such patients awake during the day were not fruitful in producing sleep at night In many cases some with disturbances of sleep, and in others without them, constantly recurring movements of the tongue and jaw, simulating yawning, were observed At times

attacks of hyperpnea thought to be due to a lesion in the quadrigeminal bodies, where the secondary centers of respiration reside, occurred There were some conditions observed which were either followed by an attack of sleep or which necessitated sleep for a disappearance of the particular condition which ensued Among such conditions may be mentioned oculogyric spasms In this condition a patient would have an upward rolling of the eyeballs, during which time an almost complete absence of will to perform motor movements would occur The spasm would last at times for many hours, and in a number of cases which I have observed disappeared when the patient fell asleep and then awakened It was a common occurrence that such patients learned at the beginning of the attack to lie down upon a couch and to fall asleep

A few cases of unusual character have been observed One that of a young lady, who following an attack of encephalitis lethargica, developed slight rigidity of the left upper and lower extremity similar to that of a beginning parkinsonian state At about this time she developed numerous attacks of narcolepsy, and noted at the same time that whenever she would laugh she would suddenly fall to the floor, perfectly conscious, but completely hypotonic. She became a person at the mercy of anyone who could make her laugh, either through the recital of a funny story, by clowning, or of tickling her This particular mechanism is characteristic of that type of narcolepsy known as Gélineau's syndrome, where in addition to attacks of narcolepsy hypotonic states produced by laughing are observed The relation of these conditions to each other is of great importance relative to speculation as to the pathogenesis of epilepsy which is characterized by some modification of consciousness

Another interesting observation was that of a young woman who, some months following an attack of encephalitis lethargica, was found unconscious on the floor of the bath-room in her home She was unable to give an explanation of her condition and with the exception of some livid marks about the neck no evidence of any disease was found A few days later her mother heard her cry out and rushing to the bath-room found her kneeling on the floor with her hands tightly clasped about her neck choking herself, and already presenting marked lividity of the face and protruding eyeballs In a few moments she lost consciousness, was carried to her bed, and remained asleep for several hours She awakened with no knowledge of what had occurred These attacks recurred at frequent intervals for a period of three years and spontaneously disappeared When questioned as to what she remembered immediately preceding the attacks, she stated that she had a feeling of an intense desire to sleep and as if someone were preventing her from satisfying this irresistible impulse

Although these several observations offer nothing definite in an explanation of the possible center of sleep, or mechanism of sleep, the association of disturbances of sleep in several directions—hypofunction hyperfunction, and dysfunction—occurring in a disease the location of whose pathology is exceedingly similar in all instances, is very significant The similarity of the somnolence due to other diseases affecting the hypothalamic region and the diabetes insipidus and adiposity common to both as well as the forced movements of yawning, seem to point to the importance of this area in its relation to sleep and its disturbances

Inasmuch as little is known of the physiology of sleep, our knowledge of insomnia is very fragmentary and nebulous Although there must be some pathologic process producing disturbance of the fundamental functions of sleep, we know very little of it It would be futile to describe the various theories of what is called insomnia They are all merely speculative, based upon observations of the effects rather than the causes of sleep and sleepnessness It will suffice to point out the conditions under which some disturbances of easy, restful, and sustained sleep occur

Insomnia may be the result of organic and of functional disease Of the former, intoxications, both exogenous and endogenous may produce a state of cerebral excitement Such intoxications may result from febrile diseases, hyperthyroidism, diabetes, at times nephritis, at certain stages tuberculosis and cirrhosis of the liver The exogenous causes may be coffee tea, tobacco, alcohol carbon monoxid, etc Painful diseases, as polyarthritis visceral disease, neuralgia may produce it Relatively mild irritations, pruritus tinnitus aurium urethritis, and nocturia are often potent causes of sleeplessness General diseases producing vascular changes in the brain, such as arteriosclerosis decompensated heart lesions, and nephritis, are often associated with insomnia Often the cause of an insomnia may be found in a Cheyne-Stokes respiration, and this is frequently overlooked Each phase of hyperpnea produces wakefulness in the patient

Hypofunction of sleep expressed as difficulty in falling asleep,

waking early, restless and unrestful sleep, and failure to sleep, all occur in functional disease of the nervous system Difficulty in falling alseep is a common symptom in all conditions of anxiety, of worry, fear, and at times melancholia One of the rather common causes of difficulty in falling asleep occurs in that type of anxiety neurosis where the patient is fearful of falling asleep lest he die during the night, and although desiring to sleep he wilfully attempts to remain awake Awaking early in the morning is pathognomonic of mental depression such as is found in the manic-depressive states It is often the first symptom of an approaching melancholia In contrast to this patients suffering with a neurosis may find it difficult to fall asleep, may wake frequently during the night, but notoriously may be able to sleep late in the morning

The complaint of not being able to sleep at all is usually the expression of a patient suffering from a neurosis In the majority of cases this supposed insomnia is really an insomniphobia At a certain period of his illness such a patient may have noted a difficulty in falling asleep because of his inability to dismiss from his mind the worrisome details of his business or other problems of adjustment If at this time, because of the difficulties of adjustment, he has become impressionable and sensitive, he has produced a fertile field for the development of fear He may have heard, read, or believed that sleep is essential to health and that if he does not sleep he will become ill, have a "breakdown," lose his mind, or what not He will become impressed with the necessity of sleep and begin to study the condition of sleep Fear that he will not be able to sleep haunts him and throughout the day he plans upon procedures to enforce sleep—hot milk, hot baths, or sedatives He attempts to fatigue himself during the day, and as night approaches becomes more and more fearful, agitated, and restless If, then, upon retiring he does not immediately fall asleep he begins to count sheep, or to read, or smoke He takes some hypnotic in increasing amount and still finds himself unable to promptly fall asleep His first thought upon awaking in the morning is that of how much sleep or how little he obtained, and he is convinced that unless he

soon is able to sleep something will occur Because of his introspection and anxiety he becomes less capable, and he interprets this in terms of mental disability

If such a patient is able to fall asleep, but wakens during the night, he may then go through the same mechanism as the patient who has difficulty in falling asleep at first In every case careful inquiry will elicit the fact that the patient's behavior is motivated by a fear of not sleeping If he can be assured that sleep is just as automatic a function as respiration, and that just as one can neither increase the rapidity of respirations beyond a certain time or stop them, so sleep cannot be denied beyond the time necessary for the proper chemical readjustment of the body that no one has ever lost his mind because of sleeplessness and that nothing can happen to him whether he falls asleep promptly or not, sleeps discontinuously or not, or wakens early or late, that he will be just as capable and that his body will in no way suffer, if he trusts the physician and is reassured he will sleep promptly irrespective of whatever adjunctive method is employed, whether it be a hot drink or muscle relaxation At times such a patient may be convinced if he is prohibited by the physician to go to sleep at all and to report the following morning That morning he is again instructed to stay awake and to perform certain activities It will be found commonly upon the succeeding morning that the patient will shamefacedly confess that he was unable to carry out the instructions of the physician because he could no longer keep awake

The administration of hypnotics is injurious, not so much because of the chronic intoxication which at times does occur, but because it is only a bad mental habit differing in no way from that of reading, walking, and smoking cigarettes for the purpose of wooing sleep In fact, many of these patients know that if they take a hypnotic they fall asleep far too soon for the sleep to have resulted from the hypnotic, and realize that they have fallen asleep only because they have been reassured that having taken a hypnotic they will sleep

The indormescent and predormescent starts are a potent factor in the development of fear of death and paralysis, but when

the innocuous character of these states is explained to the patient the ensuing insomnia disappears

As noted previously in relation to early awakening, many of the psychoses are associated with insomnia Melancholia predominantly produces bad sleep, and in this condition hypnotics must be resorted to, but must always be administered under the direct supervision of a physician When given by a nurse the nurse must make certain that the patient swallows the drug Not infrequently a patient will hoard drugs which are given to him, and swallow a large number of tablets with suicidal intent, sometimes effectually

Insomnia is likewise common in the acute psychoses with excitement or hallucinosis, and, of course, sleep is incompatible with delirium or its antecedent state of confusion, as is seen in the toxic infective psychoses Mental stupor is often observed in benign psychoses and is an instance of a mechanism of escape from reality Such an escape from reality is constantly sought by harassed patients, and attempts to sleep are a very important part of the adjustment of such patients

Where a patient suffering from ideas of a depressing nature of such a character as would normally produce anxiety and worry, is able to fall asleep promptly and to sleep well, the prognosis is usually poor inasmuch as it indicates an inadequate reaction of the organism to the emotional content of the patient So, inability to fall asleep, restless sleep, and early awakening in a patient suffering from a depression are good prognostic signs Increase of the ability to fall asleep and postponement of the time of awakening are usually precursors of the recovery of patients suffering from mental depression

CLINIC OF DR JAMES G CARR

Cook County Hospital

PERIARTERITIS NODOSA

Periarteritis nodosa was first described by Kussmaul and Maier as long ago as 1866 In the years which have intervened since that time numerous cases have been reported from widely scattered clinics and yet our knowledge of the disease remains essentially incomplete To quote the words of Spiro, "Although a half-century has passed since Kussmaul and Maier first described the clinical picture of periarteritis nodosa, and although since then almost as many cases of periarteritis nodosa have been reported as years have passed, there is still complete ignorance of the essence of the disease, an ignorance which explains the fact that almost every author who reports a case of periarteritis nodosa, in the course of his statements comes to the conclusion that every case must be regarded as worthy of publication and may be regarded as suited to bring some light into the darkness"

In 1925 Gruber collected from the literature a total of 114 cases and discussed them at length The disease is probably quite rare although it is not likely that all cases which have been observed have been reported Indeed, von Haun, in an article on the subject, refers to 2 cases which have been observed by Professor Krompecher, but not published He remarks, "Perhaps a not insignificant number of cases have failed of publication perhaps even of recognition, cases may be overlooked at autopsy or may not be recognized clinically The great difficulty of the clinical diagnosis is explained by the variability of the disease picture"

Periarteritis nodosa is a disease which is characterized by

the symptoms of sepsis with scattered local manifestations of vascular disease which baffle explanation, and anatomically, by nodular inflammatory foci in the walls of the smallest or middle-sized arteries The symptoms which occur with greatest regularity are those which are commonly associated with infectious disease, fever, leukocytosis (in this condition the leukocyte count is apt to be exceptionally high), prostration, and increasing weakness, anemia, often splenic tumor (Gruber emphasized the inconsistency of this finding), tachycardia, and various evidences of renal involvement, albuminuria, hematuria, edema, and the signs of renal insufficiency Associated with these symptoms which are fairly definite and significant are symptoms which are due to the widely scattered vascular changes within the body Doubtless the difficulty of diagnosis is more intimately connected with the latter aspect of the disease, for the wide variation of symptoms which have been presented by the cases thus far reported depends almost entirely upon the difference in location of the inflammatory nodes characteristic of the disease As Spiro puts it, "The rheumatic pains are the result of myositides due to the closure of muscular arteries, anuria, albuminuria, and even edema are the evidences of renal infarction, colitic symptoms are caused by necrosis of the intestinal mucous membrane and hemiplegic symptoms result from ruptured aneurisms of the cerebral arteries "

The clinical picture is so variable that in the great majority of cases periarteritis nodosa has not been recognized antemortem To quote von Haun again, "Cases have been regarded as trichinosis, as Werlhof's disease, typhoid, miliary tuberculosis, polymyositis, arteriosclerosis with sclerosis of the kidneys, neuritis multiplex, gastro-enteritis, pyemia, hemorrhagic nephritis, serositis tuberculosa, influenza with renal hemorrhage, purpura hemorrhagica " For instance, Hauser reported 3 cases, 2 of which were subjected to abdominal operations under mistaken diagnoses The kidneys are so often involved that hemorrhagic nephritis appears to be the most frequent diagnosis

In the cases reported by Gruber 108 were referred to in which the localization of the pathologic findings was described,

amongst these the kidneys were involved eighty times, the heart seventy-one, the liver sixty six, the gastro intestinal tract fifty, the muscles thirty two, the pancreas thirty six and the peripheral nerves twenty, the spleen and adrenals each fifteen the gall bladder thirteen, the skin and subcutaneous tissues fourteen, other organs were involved less than ten times each

The course of the disease has been regarded as leading inevitably to fatal termination Perhaps the outlook is not as hopeless as is commonly believed In Volume 227 of Virchow's Archives there are two reports of interest in this connection Spiro reports the case of a man who was under treatment for two years with recurrent ulcerations on the arms and legs He denied any venereal infection and was finally discharged as cured A month later he again came under observation because of a recently acquired syphilis For four months he was vigorously treated with mercury and salvarsan This was discontinued and five weeks later he complained of rheumatic pains Shortly thereafter albuminuria was discovered for the first time Six weeks later he had a nocturnal convulsion This was followed by many such attacks and death occurred within a short time Clinically, the case was regarded as one of cerebral syphilis Anatomically, the diagnosis of syphilis was not proved, but there was discovered a widespread periarteritis nodosa with old organized lesions and aneurysmal formation The anatomic diagnosis was, "Periarteritis nodosa obsoleta of the arteries of the heart, kidneys, liver, and intestines, small scar formations of the heart, anemic infarctions in the liver and both kidneys, extensive infarction of the intestinal wall with necrosis and ulceration hypertrophy of the left cardiac ventricle" There was no evidence, anatomically, of cerebral syphilis Spiro comments thus, "The organs supplied by the diseased arteries showed in a generally characteristic manner those changes which occur when the arterial blood supply is interrupted and no satisfactory collateral circulation is established, typical infarctions and their residue In the heart the sequelæ of foci of myomalacia, generally only microscopically demonstrable, proliferations of the interstitial connective tissue 'Cicatrices cordis', in the kidneys,

fresh infarctions with coagulation, necrosis, hyperemic peripheral zones, and a limiting line of degenerated leukocytes, the like also in the liver, in the intestine marked necrosis and extensive defects of the mucous membrane, also pictures which were to be interpreted as hemorrhagic infarctions of the intestinal wall, excessive filling of the veins of the submucosa, and the escape of blood into the muscularis and serosa" "The symptoms could only have resulted from widespread vascular disease, closure, and aneurismal formations, causing extensive injury to various organs" Spiro further comments, "This case is for the clinician the first case of periarteritis nodosa latens, for the pathologist, the first case of periarteritis nodosa obsoleta All cases of periarteritis nodosa thus far described show at autopsy the marks of a progressive process, this is the first case of periarteritis nodosa obsoleta which has come to observation and description Similar cases have been reported by Kussmaul and Maier and Benedikt-Pertel without autopsy, and by Schmorl, who did not report a histologic examination All the cases of periarteritis nodosa thus far described have been characterized by a chronic course, have lasted up to six months without the failure at autopsy of signs of an advancing process" Spiro believed that the small aneurysms discovered at autopsy were not of syphilitic origin, neither were they to be regarded as aneurysms of embolic type which had arisen in the course of endarteritis purulenta He felt that he could exclude both these conditions Von Haun reports a case with recovery, proved by examination of two nodes removed from the skin This patient was first seen in August after he had been sick for three months In November of the same year he returned to duty as a soldier Von Haun makes this statement "The microscopic picture is so characteristic that the diagnosis cannot be doubted"

These two cases from von Haun and Spiro suggest that the disease is capable of spontaneous healing, at least from the standpoint of the primary pathology Other cases of similar character have been reported While the prognosis on the basis of our present knowledge must be regarded as extremely bad, it does not appear that healing never takes place Gruber believes

that the reports of recovery from periarteritis nodosa should be received with great skepticism and reminds us of the remark of R Paltauf that the autopsy signifies the closure of the history of the disease and permits the final judgment concerning the favorable or unfavorable results of a morphologic process Gruber discusses the cases of recovery which have been reported and incidentally refers to the fact that the patient of Schmorl already mentioned died two years following the assumed recovery with acute thrombosis of the portal vein The residue of the periarteritis was found in the liver, kidneys, and heart Gruber believes that even at so late a period an acute thrombosis of the portal vein might have been an indirect result of an earlier periarteritis nodosa He believes that by all means the so called healed cases should be studied very carefully

The disease has been described in animals Jaeger carried out a careful examination of the disease in a stag, in comparison with that of a man The process is almost identical with that in the human Joest found periarteritis nodosa in the kidney of a pig Joest and Harzer have reported a second case in a pig Guldner reported the occurrence of the disease in the calf and compared it with the human Balo described the same disease in dogs where the diagnosis was made by the histologic examination of the organs of a fox terrier The nodular foci were found on the arteries of the heart

The clinical results of these vascular processes are of most interest The progress of the disease in the vessel is associated with an inflammatory deposit in the adventitia and about the vessel and in an extension of the inflammation involving the intima, resulting in endothelial desquamation and thrombosis or a proliferative inflammatory process obstructing the lumen, in some cases with organization of the vessel and in other cases with aneurysmal dilatation In either event important disturbances of circulation result Infarctions and localized hemorrhages, the latter due to aneurysmal rupture, are common Occasionally the nodes may be found subcutaneously and permit of an exact diagnosis during clinical observation The vascular changes as already pointed out account for the various manifes

tations of the disease in different organs, the simulation of nephritis, the subcutaneous hemorrhages, the evidences of peripheral gangrene, the occasional simulation of a brain tumor—all are connected with the underlying vascular disease In certain locations the rupture of an aneurysm may cause fatal hemorrhage Gruber states that neighboring tissue may be involved through a "paravascular" inflammation, that is to say, that the inflammation in the form of hyperemia, edema, exudation, infiltration, and proliferation may extend into the neighboring tissues He refers to various cases in which such findings have been found, for instance, in the cardiac muscle, in the nerves, the liver, and in the gall-bladder wall, and mentions Christeller's report of a characteristic interstitial pancreatitis as an inflammation arising by extension in the course of periarteritis

The diagnosis, as has been stated, has rarely been made clinically Except for the demonstration of the disease in an excised node, the absolute diagnosis is difficult It may be repeated that the disease presents the features of a sepsis, usually of a chronic course (lasting from six weeks to three months after the patient comes under observation), and with this sepsis there are associated changes suggestive of vascular disturbance in widely separated parts of the body These features permit of a probable diagnosis

The question of etiology has concerned many of those interested in the study of the disease Various theories have been propounded, none of which have received general acceptance Changes in pressure within the vessel, congenital weakness of the walls, nervous disturbances affecting the nutrition of the vessel walls, have been assigned as causes for the localization of the disease Not much attention is devoted to these theories now The disease is regarded as a sepsis, and more interest is being devoted at present to the question as to whether or not it is a sepsis caused by a specific organism

Spiro believes that "periarteritis nodosa is not a disease 'sui generis', the diseases which thus far have been designated as periarteritis nodosa belong in a group of processes of 'mesarteritis,' which may result after an infection of any kind"

Von Haun, on the other hand, accepts a specific infectious etiology, since he was successful in the experimental production of these periarteritis nodosa-like vascular changes in guinea pigs following an injection of a patient's blood Lemke and Sadao Otano could not repeat this experiment After an extensive consideration of various theories Gruber states his opinion thus "We regard periarteritis nodosa as the expression of a constant characteristic reactive process of the arterial system in the manner of an hyperergic phenomenon during the course of very different infectious-toxic diseases This is hypothesis!" At present we can only conclude that thus far specific etiology has not been proved, and that theories regarding the disease as a specific response of the vessels to certain types of infection are only speculation The disease is a sepsis without a proved specific etiologic factor and without a demonstrated lack of resistance to certain types of infection

Case Report.—The patient whose case report forms the basis of this study was a man of fifty three who was admitted to the Cook County Hospital June 25 1928 The diagnosis on admission was pernicious anemia with combined sclerosis For six years he had failed gradually but had no complaints except of weakness. Eighteen days ago while at work he noticed a pain in his feet which soon involved both lower extremities He had to be taken home in an automobile. By the time he arrived at home he found that the knees and ankles were swollen to a third more than the normal and were painful to touch The pain was severe starting in the sole of the foot as a burning pain intermittent, lasting for an hour or so He could obtain relief by putting the feet in cold water The pain would awaken him at night and again he would have to use the cold water The pains above the sole only came on when he attempted to walk these pains were all in the back of the leg and thigh. The swelling of the knees subsided promptly but the ankles remained swollen and tender There was a bluish discoloration and blotchy red appearance of the soles and of the toes. The pain seemed to be aggravated by allowing the feet to hang down and the onset of the pain was a feeling of heat and tingling The fingers were also painful at first but this subsided with the use of cold water They were also blue for a time.

The appetite was fair bowels regular and he had no abdominal distress no symptoms of cardiac or respiratory disorder and no urinary symptoms. The family history was negative his wife was living and well as were all six of his children He used tobacco moderately and had used alcohol to excess.

The physical examination revealed a man appearing much older than the given age. Temperature was 100 6 F pulse 104 respirations 32 blood

pressure 115/65 The head and neck were negative except for the absence of all his teeth The lungs were negative and also the heart except that the left border was located in the nipple line The liver edge was down two fingers, sharp, and tender The spleen was not palpable His finger-nails were cyanotic, there was pitting edema, and swelling of both feet, and a bluish discoloration of the toes, mottling of the legs, and arms The ankles and soles of the feet were tender to pressure

Examination of the blood showed erythrocytes 3,500,000, hemoglobin 70 per cent, and leukocytes 27,600 with polymorphonuclears 80 per cent On the day before the patient's death the leukocytic count was 18,250 with a polymorphonuclear percentage of 86 The urine was negative on two examinations, but showed a few red cells on the day before death The urea nitrogen was 13 54 per 100 mg of blood, the Wassermann test was negative The roentgenologic report read thus "Mere trace of arteriosclerosis was present anterior to the lower extremity of the left tibia None in vessels dorsal to tibiæ" The daily temperature varied from 100° to 102° F, and the pulse from 80 to 110, but was distinctly more frequent the last three days of life

Various diagnoses were made The junior house physician regarded the case as "Raynaud s disease" with some symptoms of erythromelalgia and suspected a luetic arteritis The senior house physician noted, in addition to the findings mentioned, "Dorsalis pedis artery not palpable on either foot, dorsum of either foot has a dusky hue, toes are cold, sensation upon pressure undiminished, and not accentuated, temporal vessels tortuous and sclerotic There is a systolic murmur at the apex The retinæ are normal, but the vessels are somewhat dilated and sclerotic" He offered as diagnostic possibilities Raynaud's disease and generalized arteriosclerosis On the third of July the patient was seen by a member of the neurologic staff who noted "marked tremor of the hands (intention), marked weakness of hands and feet, emaciation of hands, marked tenderness of muscles of legs, feet, and thighs Knee jerks were diminished, dorsalis pedis pulsation present, Achilles' reflexes present, lower abdominal reflexes diminished, no diminution of sense of touch or pressure, sense of position and temperature normal" His impression was that the patient had a multiple neuritis On the 6th the junior house physician noted stiffness and numbness of the right hand and forearm up to the elbow There was pallor of the index-finger of the left hand and of the entire right hand He also noted a dry gangrene of the right middle toe up to the proximal phalanx and of the tips of the third and fourth left toes At this time he found a pulsation of the dorsalis pedis arteries On the 13th the attending physician noted "drop foot and edema still present, gangrene of toes, already noted, apparently stationary There was a loss of sensation of the fingers in the right hand, marked abdominal distension, and distension of the bladder, a marked tremor of the feet, hands, tongue and mouth, also dulness over the right lower lobe with some crackling râles Diagnosis was made at this time of probable periarteritis nodosa" A surgical consultant saw the patient the same day and made a diagnosis of thrombo-angiitis obliterans

The autopsy was conducted by Professor Jaffé and revealed "periarteritis of the coronary renal, hepatic, pancreatic, suprarenal, and perisuprarenal

arteries with areas of focal necrosis in the kidneys pancreas and adrenals areas of fibrosis in the myocardium and areas of atrophy in the liver peri arteritic changes in the small arteries of the lower extremities slight hyper

Fig 178 —Periarteritis nodosa with thrombus formation (above) and or ganization (below) Section made from periadrenal tissue

Fig 179 —Periarteritis nodosa showing inflammatory destruction of wall of vessel with penetration of elastica interna and thrombus formation Sec tion from peripancreatic tissue

trophy, and dilatation of the heart, very slight atheromatosis of the aorta, subacute tumefaction of the spleen, fibrous and fibrinous obliteration of the left pleural cavity, right hydrothorax, marked pulmonary hyperemia, and edema, fibrinous adhesions between the gall-bladder and the transverse colon, and on the surface of the right hepatic lobe, beginning dry gangrene of the third and fourth left toes, slight edema of both feet" Microscopically, the anterior tibial artery showed the intima diffusely thickened with many fibro cytes Near the endothelium there were many cells filled with lipoid droplets, some of the connective-tissue fibers were covered by fine dust-like lipoid granules The smaller branches showed severe changes with perivascular infiltrations composed chiefly of lymphoid, round, and mononuclear cells These cells invaded the coats of the blood-vessels, the lumina of which became much narrowed Some of the smaller arteries were completely obliterated In the peri-adrenal fatty tissue there were found very severe changes with dense perivascular accumulations and cellular infiltrations extending from the adventitia to the intima Thrombosis was frequently seen In the cortex of the adrenals there were found areas of focal necrosis surrounded by hemorrhage Very severe vascular changes were also found in the kidneys, the liver, and pancreas, different types of which are observed, more recent ones with a complete fibrinoid necrosis of the walls and dense perivascular accumulations of luekocytes and cells with eosinophilic granulations, the older ones consisting of obliterating endarteritis and diffuse infiltrations of the vascular coats terminating in their complete destruction Thrombosis of the vascular lumina was frequent and the thrombi were often seen in various stages of organization These severe vascular changes were found especially in the kidneys, the liver, and the pancreas, and the changes described involved the middle sized as well as the smaller arteries In the pancreas and kidneys they were associated with areas of necrosis In the liver they caused the formation of atrophic foci The anterior tibial nerve showed severe disintegration of the myelin sheaths with the formation of varying sized droplets that were stained bright red with Sudan III which, in places, were taken up by the Schwann cells Periarteritis was not found in the nerve itself In the myocardium there were very severe infiltrative thrombotic and destructive changes involving the middle sized branches of the coronary arteries leading to complete obliteration of numerous branches Multiple areas of chronic myomalacia were found

Thus the case presented the typical findings of periarteritis nodosa, the symptoms of sepsis associated with widespread and bizarre signs of vascular disturbance On the basis of the history given by the patient this case ran a rapid course It might be noted that in this particular instance the signs of nephritis were not prominent, although the autopsy revealed an extensive involvement of the kidneys and the spleen, though regarded as moderately enlarged by the pathologist, was not pal-

pated clinically The leukocytosis was especially high, which is fairly common in periarteritis nodosa The anemia was moderate, but not severe

The most interesting features in this case were presented by the peripheral vascular manifestations and the signs of peripheral nerve disease The latter are of special interest Much attention has been devoted to the question of involvement of the peripheral nerves in cases of periarteritis nodosa Recently Balo reported 3 cases of periarteritis nodosa, in all of which the symptomatology was referable mainly to the nervous system In one the clinical diagnosis was tumor of the brain, in the second polyneuritis, probably as the result of alcoholism, and in the third pulmonary tuberculosis and polyneuritis Balo states that Kussmaul and Maier observed in the course of this disease paraesthesias, pains in the extremities, paralyses in the upper extremities and the trunk Upon the arteries of the muscles and nerves the periarteritic nodules were found The muscles showed fatty or waxy degeneration They regarded the changes in the muscles as the cause of the clinical symptoms In Freund's case there was pain in the extremities associated with weakness of the feet and anomalies of sensation The voluntary movements were limited without change of the passive movements The muscles were atrophied and painful Sensation was generally diminished especially toward the ends of the extremities Freund studied the sciatic nerve, the brachial plexus, and the vagus The nerves contained periarteritis nodules He found a degeneration and increase of Schwann's nuclei The same arterial changes were found in the muscles, many times with atrophy, often with necrosis In Rosenblath's case such severe pains occurred that movement was impossible Reflexes and sensation were normal The arteries of the nerves as well as those of the muscles showed numerous periarteritic nodes Ferrari, Damsch, and Beitzke, Eichorst and Gerlach made similar observations P S Meyer collected 20 cases of periarteritis nodosa with polyneuritis Kretz regarded polyneuritis as part of the characteristic syndrome of periarteritis nodosa Balo came to the conclusion that, "On the basis of our own observations we believe that the changes in

the nerves are the result of involvement of the arteries in the nerves in periarteritis nodosa The degenerative changes of the peripheral nerves must be connected with the changes in the internal organs and thus the change in the nerve is essentially a dystrophy of vascular origin" He does not accept the view that the changes of the nerves may be due to a toxic effect alone, since under such circumstances the most severe infections might be expected to regularly show nervous changes, and this has not been found in the cases of very acute periarteritis nodosa

Wohlwill believes that the changes in the nerves in the course of periarteritis nodosa are of three general types the first group is made up of cases in which the nervous degeneration appears to be due to a toxic effect alone, the second includes the cases in which extensive arterial disease is associated with very slight change in the parenchyma of the nerve, in the third group severe arterial degeneration and high destruction of the nerve are present together

Kimmestiel has also published a series of cases recently which he offered as a contribution to the still disputed subject of the coordination or subordination of the accompanying neuritis In one case, diagnosed as a polyneuritis infectiosa, there were very few changes of the arteries in the peripheral nerve, but a severe degenerative neuritis was found In a second case, in every section of all the nerves examined, there were many arteries involved in a process of severe inflammation, and in a third there were high-grade changes in the vessels of the peripheral nerves without the presence anywhere of a disease process in the nerve bundles He concludes that, "It is not to be accepted that all the tissue changes are to be regarded as the result of the vascular changes alone This is proved by the available literature concerning the involvement of the peripheral nerves, to the series of which I may add my own cases There are reports of severe, simple, degenerative changes of the peripheral nerves without arterial disease to explain such findings, then cases in which the degeneration stands in manifest association with the arterial change, and finally, my own case in which severe extensive periarteritis nodosa existed without any parenchymatous injury"

The case under discussion here serves to confirm the conclusions of Wohlwill and Kimmelstiel The degenerative processes of the anterior tibial nerve were not accompanied by a local periarteritis nodosa We have presented a case of periarteritis nodosa of rapid development and termination so far as could be determined from the history, associated anatomically with widely distributed foci of inflammation involving practically all the viscera extensively The case is also unusual in the presence of peripheral gangrene which does not appear from the literature to be of frequent occurrence The clinical signs of disease of the peripheral nerves and the pathologic demonstration of degenerative process in the nerves were not associated with vascular changes within the nerves

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THE VOMITING MECHANISM IN THE EARLY TOXEMIAS OF PREGNANCY

THE authors[1, 2] have been interested in the vomiting mechanism for some time, and are presenting in this clinic a study of a very common clinical type, the early vomiting of pregnancy We will attempt to assemble much of the recent work on the subject and present an interpretative extension of this data in the light of our experimental studies and our clinical experience gained in handling such cases as have come to us as purely medical problems The cases are selected from a group of patients that have passed through our hands in the last five years and are chosen with the thought that they will be helpful in elucidating the mechanism of vomiting We have no statistics to offer, since we have been acting in the capacity of medical consultants to the obstetricians in the care of these cases

Case I.—An unmarried woman aged twenty-eight presented herself to the clinic complaining of underweight anorexia fulness after eating which was associated with nausea and occasional attacks of vomiting She was 5 feet 8¼ inches tall weighed 104½ pounds. When compared to the average individual of her height and age she was 42 per cent. underweight She was an unusually active girl and corresponded to the class of people designated as suffering from constitutional thinness Her digestive capacity seemed to be below her metabolic requirements. She entered the hospital January 28 1927 and was studied most carefully No organic basis was found for her complaints.

Pre-insulin Period.—This period extended from January 28th to June 29th five months. She was requested to rest most of the day but was allowed to take a short walk in the afternoon in order that she might get fresh air At no time did she do any significant work. It was proposed to determine in this period whether she could be fattened by reducing her activity

and forcing on her a maximum quantity of food Her basal requirements were 1360 calories During four and a half months of this time she was served a diet which varied between 2720 and 3400 calories It was found if she pushed the food intake beyond a given amount that she would become nauseated and vomit On her best days she was rarely able to eat over 3000 calories which corresponds to a basal plus 117 per cent At the close of this period she weighed 110 pounds, a gain of 5½ pounds in the five months

Insulin Period—On July 1st she began taking insulin and eating her prescribed diet At first the dose was 10 units twice daily, but this had to be lowered to 7 units twice daily Her activity was increased somewhat Her diet was not weighed during all of this period, but on the average it was in excess of 3000 calories, the quantity taken in the previous period The nausea, fulness, and distaste for food were replaced by hunger On September 12, 1927 she weighed 120 pounds, a gain of 10 pounds in two months and twelve days This more rapid gain in weight was not so significant as the complete change in the patient's general health and disappearance of her symptoms

The senior author[1] has emphasized the fact that there is an intestinal phase to the vomiting act This phase finds its motor expression in a reversal of the peristalsis and the pathologic regurgitation of duodenal contents into the stomach Simultaneous with this motor activity the patient experiences the sensation of nausea This sensation was regarded as the sensory expression of the duodenal dysfunction Clinical experience and experimental evidence are a unit in the opinion that the stomach may retain surprisingly large quantities of material during these periods of nausea In some cases the patient may be annoyed by esophageal regurgitation, in other cases the quantity of material remaining in the stomach may not be large, but the analward peristaltic waves may be absent

Alvarez[3] has discussed this phenomenon of reverse peristalsis and has indicated that lesions of the rectum, lower bowel, and pelvis may be powerful in initiating it He has conceived of a metabolic gradient[4] existing along the gastro-intestinal tract which is a determining factor in the direction and the vigor of the peristaltic waves It is highly probable that such a condition of gastric stasis existed in this patient in the pre-insulin period and was responsible for her symptoms It is, of course, a well-established fact that following the administration of insulin the blood-sugar is lowered, and this hypo-glycemic reaction induces hunger in the patient Bulatao and Carlson[5] have shown that

this hypoglycemic reaction induced by insulin not only strengthens the individual gastric contractions of the empty stomach, but also augments the tonus so that frequent periods of hunger tetany exist On the basis of Alvarez's conception of metabolic gradient the stomach under stimulation of insulin would be an area of high metabolic activity In other words, a normal analward peristalsis would replace the gastric stasis or reverse peristalsis It can be seen that it is not necessary to attribute the beneficial effects of the insulin in this case to some undefined defect in the carbohydrate metabolism Its use was a physiologic device by which a vicious circle was interrupted Clinically speaking, it was a form of symptomatic treatment

Case II.—A woman aged thirty two primipara entered the hospital January 14 1928 Her past history was not remarkable She had vomited for one week prior to entrance and at the time was keeping down very little food Her tongue was a little dry The urine contained a trace of albumen acetone two plus diacetic acid zero The blood-counts were within normal limits.

She was placed on a diet containing 1727 calories divided into three dry meals which were followed in two hours by fluids Ninety grains of bromide were administered daily per rectum in two doses. Between the 14th and 28th she retained most of her food with sporadic vomiting attacks. However she was always on the verge of vomiting

On the 28th her weight was the same as on admission She was then given 5 units of insulin twice daily This dose was later increased to 7 units. From this time onward her improvement was definite The bromides were discontinued and she was allowed out of bed daily She was discharged February 6 1928 eight days after insulin administration was begun The injections were continued for five to six weeks Her strength returned rapidly and the further course of the pregnancy was uneventful

Here, then, was a patient who had a relatively mild degree of vomiting which was rapidly developing into the severe type, "hyperemesis gravidarum" With the standard treatment used in such cases she made questionable progress If she had been sent home in this state she would most certainly have suffered a relapse The use of the small doses of insulin was an important factor in her recovery The authors have seen 3 other cases improve definitely and recover under the use of insulin after the oral and rectal administration of bromids had proved ineffective

It is, of course, quite obvious that when one institutes insulin administration, there should be no doubt that the patient is able to retain sufficient carbohydrate for protection against the dose given

This raises the much discussed question of whether, after all, the fundamental defect in this type of vomiting is not some error in carbohydrate metabolism This is a difficult question to answer, because once the vomiting has begun, its secondary effects on the organism are far reaching Thus, a patient who persistently vomits develops a state of starvation, a consequent ketosis, an acidosis or an alkalosis, and a dehydration of varying degrees

Duncan and Harding[6] were impressed with the beneficial effect obtained by feeding to these patients large quantities of carbohydrates If the patients were unable to retain the carbohydrates by mouth, glucose was given subcutaneously These authors also noted fatty degeneration in the livers of those cases coming to autopsy These degenerations were attributed to carbohydrate deficiency So they concluded that this vomiting or toxemia was attributable to a defect in the carbohydrate metabolism

Later, Harding and Potter[7] considered that these patients were to be regarded as suffering from starvation Since, however, the requirements for carbohydrates were much greater in the pregnant woman than in the normal individual, a deficiency was a more serious matter In a still later article Harding and Wyck[8] have emphasized the rôle of dehydration It will thus be seen that the attention of these workers has gradually shifted from the conception of an existence of a fundamental defect in carbohydrate metabolism They are now stressing the rôle of the carbohydrates in correcting the complications arising out of the vomiting Titus, Hoffman and Givens,[9] and Miller[10] have championed the view that a fundamental error exists in the carbohydrate metabolism They arrived at this conclusion for the same reasons as those advanced by Harding and associates In addition, Titus has reported the existence of an actual or relative hypoglycemia in his toxemic patients His findings in

this respect have not been corroborated by Stander [11] Thalhimer[12] has been an outstanding advocate of the use of insulin and glucose administration However, he is obviously treating cases which present the complications of ketosis and dehydration

In the milder cases, such as Case II, in which the complications have not occurred, insulin alone seems to be helpful It does not seem necessary to consider its action as specific on the carbohydrate metabolism, but rather as a form of symptomatic treatment which increases the hunger contractions This view has been expressed by Sachs[13] and Vogt,[14] and is the one adopted by the authors Stander has reviewed the entire controversy in which many investigators have engaged, and he concludes that there can be little doubt that the changed metabolism accompanying pregnancy, which may so easily become prevented, is the underlying cause of all cases of vomiting of pregnancy He further states that apparently we do not know the starting point of this changed metabolism, but it seems rational that in the treatment we should endeavor to restore the patient to a normal metabolism So far he concludes that the best therapy to this end seems to be the use of insulin and glucose

From the consideration of the above it is perfectly obvious that one should, if possible, divide his cases into two classes

(*a*) Mild cases of vomiting without significant ketosis and dehydration

(*b*) More severe cases in which significant ketosis and dehydration have occurred

As Stander suggests and is apparent to all workers, the pregnant woman does develop these complications very readily Once they appear, there is no doubt of the etiologic rôle of the carbohydrates in their production, nor of the necessity for the use of carbohydrates in combating these states

Case III.—The patient, aged twenty four primipara menstruated last on March 9 1926 and became nauseated on April 15 1926 The nausea was associated with epigastric pain described as a squeezing pain. She had a pain in the left side of her abdomen also which radiated down the front and outer side of the left leg The nausea and epigastric pain grew progressively worse until May 17 1926 when it was necessary to hospitalize her

Her past history showed that on two occasions within the last year she

had had attacks of nausea, vomiting, and epigastric pain The last one followed three days after the onset of a cold She recalled that she always vomited easily as a child, and was frequently nauseated The pain which radiated into her leg had also been present before, but she usually attributed it to rheumatism, and for this reason did not attach much significance to it There were no symptoms referable to the urinary tract other than a nocturia (twice)

On examination she presented evidence of a beginning dehydration, pulse 90, temperature ranges 98° to 99 2° F , respiration 22, blood-pressure, systolic 110, diastolic 80 tenderness in left side of abdomen and left lumbar region Urine contained acetone 1+, and was negative otherwise Vaginal examination confirmed an early pregnancy

After a study of the case it was decided that the patient probably had some urinary pathology It was considered that an obstruction existed in the left ureter and that the radiations of pain down the leg were ureteral in origin On cystoscopic examination, a No 5 catheter met obstructions at 5 cm and at 15 cm , on the right side, a No 6 went easily to the kidney on the left The left urine was sterile The right urine contained a short chained streptococcus (Streptococcus viridans) Pyelograms were not made It was felt that the injection of the radiographic material would irritate the ureter and kidney pelvis, aggravating the vomiting As a matter of fact, the vomiting was aggravated for twenty-four hours and then gradually lessened Seven days later the No 6 catheter was passed to the right kidney, with difficulty, but a No 7 went easily to the left One per cent mercurochrome was instilled into each kidney pelvis The reaction was again stormy, with a return of vomiting However, she was able to leave the hospital four days later eating adequate quantities of food For twenty-four days she had no abdominal pain and no further vomiting attacks When these returned the ureters were again dilated The further course of the pregnancy was normal Pyelograms were not secured after delivery

Case IV —The patient was a primipara aged twenty-one Her last period was July 12, 1927 Nausea began September 20th On October 10th she caught cold and her vomiting increased She entered the hospital October 14th with a temperature of 99 2° F , pulse 104, respirations of 22 She appeared severely sick. She was vomiting everything taken and complained of pain in the lower abdomen On examination the left kidney was somewhat tender Blood-pressure was systolic 100, diastolic 75, urine contained a trace of albumen, acetone ++, and diacetic acid + The red blood-count was 2,600,000, hemoglobin 50, and white blood-count 12,500

She was given 1000 c.c of 5 per cent glucose subcutaneously every eight hours and bromides were used in large doses per rectum With this treatment the albumen disappeared and the ketosis cleared Four days after admission, on cystoscopic examination, only a No 4 catheter could be passed on the left A No 6 went easily to the kidney on the right Thirty-six hours later the patient was still vomiting The sclera had become subicteric in color Since the red blood-count was already quite low a therapeutic abortion was advised and performed at once, which was followed by rapid recovery of the patient

Two and one-half months later a complete urologic study was made This showed a right sided hydronephrosis with a ureteral stricture a left sided irregularity in the pelvis suggestive of an infection From the right ureter a Gram-positive coccus was obtained and from the left a Gram positive bacillus. Both ureters were then dilated at intervals of two weeks up to a No 10 bougie

Second pregnancy This pregnancy began in November 1928, and terminated August 7 1929 She had periods of nausea up to the fourth month, but she did not vomit. She had no backache and an uneventful pregnancy from the fourth month until delivery

These 2 cases might be classified as cases of pyelitis of pregnancy Neither one presented any appreciable temperature, or any symptoms of dysuria In the one the ureteral pathology was recognized by the tender kidney and the reference of pain to the leg In the second case the lower abdominal pain and tenderness in the left kidney might have escaped attention except for our former experience These cases correspond in their behavior to those described by Hunner[15] in 1925 Some of the urologists have spoken of these as silent infections of the kidneys They may be silent as to the evidence of infection, but they are stentorian in their effects on the vomiting mechanism

As would be expected, the outspoken cases of pyelitis associated with pregnancy first received the attention of the urologists and obstetricians There are numerous reports in the literature of the value of ureteral dilatation and the use of indwelling catheters The most recent reports which contain references to the literature are those of Stevens and Henderson,[16] Pugh,[17] Corbus and Danforth,[18] and Hirst [19]

It next became apparent that practically all pregnant women present some degree of obstruction to the ureters Kretschmer and Heaney[20] reported the dilatation of ureters of women at term More recently Duncan and Seng[21] have shown in women who gave no history of infection that the ureters showed beginning dilatation between the sixth and tenth week of pregnancy

The nature of this obstruction has been investigated by Hofbauer [22] He has shown that hypertrophic and hyperplastic changes exist in the juxtavesical portion of the ureter but he

believes that the congestion and edema of the mucosa also contributes to this obstruction Associated with these constant findings of obstruction and dilatation there is evidence of loss of tone to the ureter and insufficiency of ureteral peristalsis In other words, even an uncomplicated pregnancy establishes physiologic conditions favorable to urinary stasis There are indeed few normal women who pass an entire pregnancy without harboring at some time a focus of infection Hence, the findings of Duncan and Seng[21] that 42 per cent of their antepartum cases showed evidence of infection is not surprising Indeed, one would suspect that it would be the exceptional case that has passed four months of a pregnancy with a urine incapable of giving a positive culture at some time

Case V —This case is remarkable because of the long period of observation and of the various types of managements that were used in her five pregnancies

First Pregnancy —She was twenty-seven years of age at her first pregnancy Her last period occurred August 6, 1924 Nausea began September 5, 1924 and on September 9, 1924 she was admitted to the hospital with the history that no food or water had been retained for three days Her urine showed albumen, acetone, diacetic acid, and casts Her blood showed a carbon dioxid combining power of 50 The blood-pressure was not elevated For five days she was treated by the use of fluids and bromids per rectum, atropin, grains $\frac{1}{150}$, hypodermically, and forced feeding of carbohydrates She made no progress

She was then given glucose intravenously and subcutaneously, followed by 10 units of insulin This treatment caused sufficient improvement to allow the patient to retain food by mouth after the liberal use of bromids She was discharged from the hospital eighteen days later in good condition

Two months later, December 10, 1924, she developed a spontaneous miscarriage She was advised to have two devitalized teeth extracted before attempting another pregnancy

Second Pregnancy —The patient entered the hospital August 6, 1925 stating that she had been vomiting for four to five weeks She remained in the hospital eight days During this time she was returned to a good metabolic state by the use of a dry diet followed by fluids two hours later and liberal use of bromids. At no time was there an elevation of blood-pressure A spontaneous miscarriage occurred about six weeks after leaving the hospital

Third Pregnancy —She was first seen on May 14, 1926 complaining of loss of weight and vomiting Her last period was March 21, 1926 At this time the vomiting had not become pernicious. The examination showed a normal temperature, pulse, and blood-pressure The left side of the abdomen was somewhat tender and there was slight urinary frequency during the

day, but no nocturia At this time the authors had become impressed with the etiologic rôle of the kidneys and ureters in the production of these intractable forms of vomiting So a cystoscopic examination was made although there were no definite symptoms pointing to the urinary tract. The urine from the left ureter showed a colon bacillus infection associated with a ureteral dilatation and kinking as shown in the pyelograms (Figs. 180 181)

She developed a sharp reaction with severe vomiting but was able to leave the hospital the day following Seven days later May 21 1926 she

Fig 180.—Left pyelo-ureterogram.

received a dilatation This was followed by such severe vomiting that she was readmitted to the hospital Under bed rest bromids and forced feeding the vomiting quickly subsided On May 31 1926 another dilatation was done which was followed by sporadic vomiting for four days. On June 12th she was discharged in good condition One other dilatation was done, which did not necessitate her return to the hospital On December 13 1926 she was delivered of a baby girl.

Fourth Pregnancy.—In the spring of 1927 the patient developed a severe backache which was relieved by three ureteral dilatations. On October 11 1927 she had a normal period. On November 17th she had a scanty period and on November 25th she began with morning sickness. This vomiting

gradually increased in severity Her blood-pressure was 120/90, pulse 92, and weight 110 pounds The urine contained albumen, acetone, and on culture, streptococci were obtained from both kidneys She was admitted to the hospital and dilated on the 7th, 15th, and discharged on the 19th in good condition She remained in good condition until December 21st, when she developed a cold with a severe cough and diarrhea The vomiting gradually returned, so that she was forced to enter the hospital on January 10, 1928 At this time she was dehydrated and had a well-established ketonuria She was given 1000 c c of 5 per cent glucose subcutaneously every five hours Following the first administration she developed from 10 to 20 Gm of sugar

Fig 181 —Right pyelo-ureterogram

in the twenty-four hour specimens of urine Insulin was added in gradually increasing doses, so that she was getting 30 units to 1000 c c of fluids and 50 grams of glucose The ketonuria and dehydration disappeared, but the patient continued to vomit On January 19, 1928 ureteral catheters were passed and in three days she was taking adequate quantities of food and fluids by mouth It was then decided to administer the insulin in doses of 7 units twice daily and to follow each dose with a meal heavy in carbohydrates She was dismissed from the hospital on this regime and continued on it for six weeks

There were no further vomiting attacks and she had a spontaneous delivery of her baby at eight months. The baby is living and well

Fifth Pregnancy—The patient was not seen in this pregnancy but she has made the following report so that her record might be brought down to date. Pregnancy began the latter part of February or the first of March Nausea and vomiting were severe. She received the usual treatment (bromides dry high carbohydrate diet etc.) given in such cases but she had no ureteral dilatations no insulin and no parenteral injections of glucose. She miscarried spontaneously on April 6 1929 In the short intervals between her pregnancies the patient could not be interested in taking sufficient treatments to correct her condition

This patient has passed through five severe periods of early toxemia In each case the severity was such as to claim the designation of pernicious vomiting On two occasions the prognosis as to life was definitely doubtful On the standard conservative treatment with a high carbohydrate diet insulin and glucose glucose alone and the liberal use of bromids she developed three spontaneous miscarriages.

On the same treatment combined with repeated ureteral dilatations she was delivered at term of a living baby in 1926

On ureteral dilatations plus the protective use of glucose and insulin when ketosis and dehydration appeared plus the routine use of small doses of insulin followed by her prescribed diet she was delivered of a healthy baby in 1928 at eight months which is now living

From many sources[23] are coming reports of the beneficial effects of ureteral dilatations in the toxemias of pregnancy Kahn,[4] who apparently has studied chiefly the late toxemias of pregnancy (52 cases), states that as the renal involvement abates the toxemia diminishes Hirst[19] concludes that early and late toxemias are essentially different, the latter is primarily of renal origin

SUMMARY

The authors wish first of all to emphasize that in the average early pregnancy there are sufficient changes in the pelves of the kidney and the ureters to act as powerful reflex stimuli on the vomiting mechanism If in this average pregnancy a chronic focus of infection exists or an acute upper respiratory tract infection develops, then the probabilities that the urinary tract will exert reflex effects on the vomiting mechanism are increased

It is, of course, apparent that the vomiting mechanism may be stimulated from other reflex fields (gall bladder) and by other associated conditions, such as a thyrotoxicosis However, one must regard these as accidental associations The conditions,

arising in the pelves of the kidney and the ureters, on the other hand, are the direct sequelæ of the pregnancy and do not of necessity arise in its absence For this reason it is evident that the urinary reflexes must be given major consideration in analyzing the mechanism of vomiting in the "early toxemias"

If the pregnant woman once begins to vomit she rapidly develops a vicious cycle with the complications of dehydration and ketosis Glucose without the use of insulin usually controls the ketosis Occasionally a patient will be found (Case V, fourth pregnancy) in whom the subcutaneous administration of glucose results in a glycosuria Insulin mixed with the injected fluid is helpful in controlling this glycosuria Loeser[25] says that in these severe cases the liver has lost the power of glycogenesis and that the insulin restores this property to the organism Such a defect would be a secondary one as the result of liver damage All the evidence which has been adduced for the existence of a defect in the carbohydrate metabolism indicates that this defect arises only after the complications develop

It is suggested that the benefits which a pregnant woman derives from the use of small doses of insulin given twice daily is the same that comes to a non-pregnant woman with a tendency to anorexia and nausea unassociated with an organic etiologic factor The insulin increases the gastric hunger contractions, reverses the peristalsis, and abolishes the nausea consequent upon the intestinal antiperistalsis and duodenal dysfunction

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BRUCELLA ABORTUS INFECTIONS IN MAN (UNDULANT FEVER)

SINCE the first human case of infection with Brucella abortus in America was reported by Keefer[1] in 1924 an increasing interest in this disease has been manifest in the literature Many points regarding its clinical manifestations, its relation to Malta fever, and the significance of the serologic and bacteriologic tests are still open for discussion Even the name of the disease is not constant in the different studies The more recent articles show a tendency to talk about "undulant fever" and to ascribe the American cases to the "abortus type of Brucella melitensis" (Hull and Black,[2] Hardy,[3] Farbar and Mathews[4])

Clinically, the disease as described in America bears a striking relation to classical descriptions of Malta fever (Heiser[5]) The clinical picture is so varied that we find it exceedingly difficult to give a description accurate enough to make the diagnosis without laboratory help This condition seems to be true in what we are able to read of Malta fever There are certain types or stages of fever in America (Sensenich and Giordano[6]), the true undulant apparently is the least common The complaints of the patient are extremely variable, and, on the whole, are general in character such as weakness, sweating, chills or chilliness general malaise, joint pains, indefinite gastro intestinal symptoms and headache There seems to be no specific syndrome of symptoms Physical signs likewise are indefinite an enlarged spleen and leukopenia are perhaps the most common (Hardy[3])

The diagnosis of Brucella abortus fever then rests on laboratory tests If Brucella melitensis or Brucella abortus is isolated from blood culture the diagnosis is made Frequently, however, the patient's symptoms are so mild that his blood is not cultured, or at least not under anaerobic conditions, and Brucella abortus, the more common strain in America, is not obtained, since it grows with difficulty on initial isolation under aerobic conditions Morphologically and culturally, Brucella melitensis and Brucella abortus are similar Both are non-motile, Gram-negative, pleomorphic bacilli, and neither ferments carbohydrates Huddleson[7] differentiates the two strains by gentian violet medium (Brucella abortus is inhibited by 1 50,000, while Brucella melitensis is not inhibted), but other investigators have not found that method successful in their hands The diagnosis must, then, rest on serologic tests Evans'[8] method of differentiating the strains by specific agglutinin absorption has been the most successful

As one analyzes the literature one becomes impressed with the essential unity of the two organisms Malta fever is a disease caused by Brucella melitensis which has passed through goats, Brucella abortus infection is caused by the same organism which has passed through cattle or perhaps swine (McAlpine and Slanetz[9]) The discussion regarding the relation of swine to undulant fever is becoming increasingly important in the epidemiology of the disease

Brucella abortus is the organism causing infectious abortion in cattle It is surprising that the first effort to find evidence of this disease in man dates from 1913, when Larson and Sedgewick[10] studied the complement fixation reaction of the blood of 425 children and found 17 per cent positive Most of the later serologic work deals with the agglutination reaction Some investigators (McAlpine and Mickle[11], Giordano and Abelson[12]) have performed a routine agglutination on all blood specimens sent in for Widal typhoid tests, so that now thousands of such tests have been reported A negative test does not exclude undulant fever, nor does a positive test necessarily imply that the individual has the disease This will be discussed later

None of our patients died, and we have had therefore, no experience with the pathology of the disease An animal experiment showed lesions that are similar to those found in tuberculosis, sometimes even to those seen in rickets If, as some students believe, guinea pig inoculations of patients' blood will become one of the diagnostic procedures, the increased familiarity with the pathologic lesions will be of considerable importance

We have been able to make a fairly intensive study of 5 positive cases. We shall give a very brief clinical outline of each case, emphasizing especially those features that in the obscurity of the moment seem most important The serologic studies will be grouped together

Case I.—A young woman of twenty six a social worker was first seen in August, 1927 with an illness dating back six weeks Symptoms were weakness fatigue and headaches, chills epigastric pain and pain in the shoulders occurring two weeks ago The shoulders became red tender and swollen There was a daily temperature of 99 4° to 100 F Nothing else was found The joint symptoms cleared up in two weeks The patient continued to have fever and left the hospital of her own volition The discharge note read patient had acute arthritis but this diagnosis does not explain all her symptoms At this admission all laboratory tests were negative including two blood-cultures.

After leaving the hospital the temperature rose daily to between 99° and 101 F and she was always tired She returned to the hospital two months later for further check up and again nothing was found Despite the fact that no positive evidence of tuberculosis could be found anywhere this diagnosis was suspected and the patient was told to stop work and to spend the winter in California. Out there she entered a hospital and had another survey which was negative

She returned to Chicago in the spring of 1928 Apparently she had fever all the time and in July it occurred to us that she might have an abortus infection The first agglutination test was positive 1–1280

Case II.—Mrs. J M aged twenty three came to the office July 5 1928 on account of a fever of nine months duration About nine months ago her husband had typhoid fever one day after visiting him she caught cold and had temperature of 103 F with some abdominal pain This was diagnosed as appendicitis. She had daily temperature of 99° to 100 F On October 19 1927 appendectomy was performed which was followed by a six weeks period of normal temperature. Since then she has had a temperature of 99 to 100 F all day without any other symptoms except some distress from a cervicitis.

Hospital examination was negative except for a positive macroscopic

agglutination of Brucella abortus in a dilution of 1 320 and of Bacillus typhosus in 1 40

Case III —Patient of Dr Karl Tannenbaum, aged twenty-seven, husband of the last patient, had had a short course and somewhat anomalous typhoid fever at St Luke's Hospital from October 4 to 21, 1927 Bacillus typhosus was obtained from the blood-cultures, and Widal tests were positive during that time Agglutination with Brucella melitensis, Brucella abortus, and Bacillus alkaligenes was negative

He had been in perfect health since his attack of typhoid, but because his wife's illness dated from a visit to him, he was asked to come to the laboratory for tests He showed a positive agglutination of Brucella abortus in serum dilution of 1 320, positive for Brucella melitensis in 1 40, and negative agglutination for triple typhoids

Case IV —A patient at the Medical Clinics, University of Chicago, service of Dr Bay, a medical student, aged thirty-three, entered the hospital in December, 1928, during a severe epidemic of the respiratory disease generally called "flu" His temperature, instead of showing a steady decline, started to drop, and then presented an ascending curve of a remittent type There was also a period of apyrexia, followed by another wave of fever Physical examination was negative, the spleen was not palpable A blood-culture showed Brucella abortus, agglutination was positive

Case V —A woman, aged forty-eight, service of Dr Sidney Strauss, Michael Reese Hospital, entered January 19, 1929, complaining of painful joints, loss of weight, nervousness for three months There was apparently a true arthritis, involving most of the large joints She had lost 45 pounds, and for a few days before admission had had fever There was no previous history of arthritis Her last menstrual period was three weeks before her admission to the hospital and was three months late She had cramps and passed clots The period lasted nine days She had had twelve pregnancies, the first of which was a spontaneous abortion at four weeks In the dispensary a basal metabolic rate of plus seventy-six was found and hyperthyroidism was considered the probable diagnosis

In the hospital it was noted that her joints were painful, red, and swollen The tonsils and teeth were in bad condition The diagnosis of acute arthritis was made A low-grade fever and tachycardia were present Salicylates in large doses had no effect on either the temperature or the arthritis, and on February 13th injections of milk were begun The first injection was made with certified milk and the subsequent injections with boiled milk. After one injection of 7 c c , there was a chill, temperature of 103° F , exacerbation of the joint pains, followed by the development of a small fluctuating mass at the needle site Eighteen days after this injection the first agglutination tests were done and were positive for Brucella melitensis in 1 320 dilutions, but were negative for Brucella abortus In this case the white count was between 10,000 and 16,000

A blood-culture taken on February 3d after five days contained a few

small Gram negative bacilli that did not grow on subculture. Another blood culture taken on April 22d revealed similar Gram-negative bacilli that were non motile These bacilli were agglutinated in high titer by a known Brucella melitensis immune serum

Immunity tests were performed with the serums of the cases reported The melitensis strains used for antigens were as follows Four strains were obtained from the American Type Culture Collection, and were as follows a strain of Brucella abortus (porcine) and Brucella abortus (bovine), one strain of Brucella melitensis (human), and one strain of paramelitensis These cultures were sent to the Collection by Huddleston, who in turn had received them from Evans Another strain was obtained from the New York Board of Health—Meyer strain eighty of Brucella abortus This strain has been found to be highly agglutinable and to have low virulence, and, accordingly, it has been used for serologic tests throughout the country The sixth melitensis strain was obtained from Billings Hospital, a freshly isolated strain from our Case IV that was bacteriologically and serologically the Brucella abortus type

The macroscopic agglutination test was employed through out Agglutination tests had been performed in such numbers on normal serums that only a few were included for controls in the series reported Fifty serums were tested 7 gave positive agglutination and 43 did not agglutinate the melitensis strains The negative serums included those from patients in whom undulant fever was suspected and from patients with a variety of other diseases The latter group was included in order to judge of the specificity of the agglutination test This negative group of serums included those from patients with typhoid fever (blood, urine, and stool cultures positive), from patients with bronchial pneumonia, from chronic colitis, from tonsillitis, from actinomycosis of the lung, from endocarditis, both rheumatic and subacute bacterial from tertian malaria, rheumatism, nephritis lung abscess, pleurisy, and syphilis

It is apparent, therefore, that the agglutination test for strains of melitensis is comparable in its specificity to that of agglutination for typhoid, since the serums giving positive tests

were from patients in whom the clinical findings were compatible with fever due to Brucella abortus, and since serums from normal persons and from patients with other diseases contain no agglutinin for melitensis strains The agglutinin titer of the serum was sometimes identical for Brucella melitensis and Brucella abortus An absorption agglutination test determined the specific strain in such instances

Opsonic index The opsonic indices were determined in the serums that had given positive agglutination tests with melitensis strains A few serums from healthy persons were included as normal controls and a few strains from patients with other diseases in order to test its specificity The results of the opsonic indices with the serums giving positive agglutination tests were as follows With Brucella abortus, 5 2, 1 6, 4, and 5 4, with Brucella melitensis the corresponding indices were 4 7, 1 1, 2 2, and 2 3 The opsonic indices from the control serums were usually under 1, 1 1 was the highest The opsonic index, therefore, appeared to be specific for the melitensis group and showed more strain specificity than agglutinin determinations, it should prove, therefore, a useful diagnostic test in suspected undulant fever Opsonin, like agglutinin, persisted in positive serums for at least eighteen months after the patient's symptoms had subsided, for example, the first case reported had an opsonic content of 2 7 after a year and a half

Phagocytic index The phagocytic activity of the patient's leukocytes for melitensis strains was examined in several cases, giving positive agglutination The phagocytic index was always found to be considerably increased

Complement-fixation test Complement-fixing antibodies were also investigated Normal serums and typhoid immune serums were used for controls The control serums were negative in every instance The serums from the cases reported gave strongly positive complement-fixation tests when examined shortly after the acute symptoms, and weakly positive complement-fixation tests when examined after a year In the few serums examined it was impossible to determine whether the patient had a Brucella abortus infection or a Brucella melitensis

infection Either the simple antigens (killed bacterial suspensions) were not delicate enough to differentiate the strains or the complement-fixation test is group specific, but not strain specific Further tests using absorbed serums and more refined antigens might prove more valuable

It is apparent from even the few serums examined that the immunity reactions as illustrated by agglutinin, opsonin, and complement fixing antibodies are a valuable aid in diagnosing melitensis infections and that the agglutinin absorption test differentiates the Brucella abortus and Brucella melitensis strains Although the opsonic test shows more strain specificity than the other reactions, nevertheless, the agglutination test would probably be the one of choice for routine examination for undulant fever, since the test is clear cut, specific for melitensis strains, and since all laboratory assistants are familiar with the typhoid agglutination test to which it is similar

Several preparations were employed for intradermal tests A vaccine, a filtrate, and a filtrate from a frozen and thawed culture (32) The culture medium used for the preparation was a sugar free veal infusion broth, 1 per cent peptone, Ph 7 4 Portions of the cultures were examined at intervals varying from two to seventeen days In preliminary tests the potency of the filtrates was examined by the intradermal tests in guinea pigs Filtrates of uninoculated medium incubated for the same length of time were used for controls in the same dilutions as the filtrates The skin reactions with the preparations were barely perceptible in guinea pigs, and it was, therefore, necessary to immunize the guinea pigs in order to obtain positive tests According to the guinea pig tests the most potent filtrate was obtained from seventeen-day cultures, frozen and thawed and filtered Both filtrates gave more positive tests than the vaccine The vaccine was a washed, twenty four hour culture of the melitensis strain It was suspended in physiologic salt and standardized to one billion per cubic centimeter The tests on guinea pigs were not considered very satisfactory and several healthy volunteers submitted to the intradermal tests The results were negative Whenever a patient's serum showed agglutinin for either the

melitensis or abortus strains an intradermal test was made with one or more of the preparations These tests were uniformly positive When the filtrate was injected an urticarial wheal and erythema appeared about the needle site within a few minutes This reaction was either slighter or absent after the injection of the vaccine A reaction which was considered positive appeared definite within eighteen to twenty-four hours and persisted for at least forty-eight hours A strong positive reaction had an elevated dark red, indurated center at least 2 cm in diameter and frequently surrounded by a less definite but circumscribed halo of 3 to 4 cm A weakly positive reaction consisted of a reddened indurated area 1 to 2 cm in diameter and not surrounded by the halo The intradermal test with filtrates apparently contained more of the potent substance than did the vaccine Judging from the skin tests in the patients who had given positive agglutination tests and from the intradermal tests in a few healthy persons, it seemed possible that this test might prove a diagnostic aid in undulant fever However, in a larger series of intradermal tests in normal persons and in persons with various diseases, a number of weakly positive reactions were encountered and one very strongly positive reaction This strongly positive test was obtained in a healthy person, his serum was examined for agglutinin and opsonin, but was entirely negative for both The weakly positive reactions were usually obtained in patients having a slightly elevated temperature, and the reddened area usually faded after twenty-four hours Control skin tests were made in each instance with either a typhoid filtrate or a filtrate used by a physician from another hospital The latter tests were also weakly positive in many instances

In view of the one strongly positive skin reaction in the healthy person without history or symptoms or other immunity reactions, and in view of the weakly positive reactions (25 per cent) in other persons without apparent past or present melitensis infections, the positive intradermal reaction with the preparations of Brucella melitensis and Brucella abortus is at present of little significance or aid in diagnosing undulant fever

ETIOLOGY

The etiology of the cases reviewed is indefinite

Case I.—This young woman had lived in Iowa most of her life and had frequently consumed raw milk. Many cases of Brucella abortus have been detected by Hardy in Iowa. However, the woman had lived in Chicago for at least one year before her first admission to the hospital and has, as far as she knew, drunk pasteurized milk only.

Case II.—This patient and her husband (Case III) had spent six weeks in one of the national parks before her husband had typhoid fever and before she had fever (undiagnosed). Although they were staying in a hotel, it is quite conceivable that they may have had raw milk during some of their trips about the park.

Case IV.—This young man was convinced that he had contracted the disease from drinking raw milk. His family had not liked the town milk and had had a cow sent in from the country (Ohio). He promised to send a sample of the cow's blood, but as yet it has not been received.

Case V.—This woman, as has been mentioned elsewhere in the report, received non-specific protein injections of milk. She may have contracted Brucella melitensis from the milk or she may have entered the hospital with an arthritic type of undulant fever. Tests for Brucella melitensis in the milk were negative.

DISCUSSION

It is quite apparent that these patients may not all be cases of undulant fever. Case IV is the only typically acute febrile case with positive blood culture. Case I, with all other findings negative, belongs, in all probability, to the ambulatory type of undulant fever. Case II, and her husband, Case III, are particularly interesting because both date from the latter's typhoid fever and there can be little reason for doubting the accuracy of this diagnosis. Why both husband and wife should show a positive Brucella abortus agglutination a year later is somewhat perplexing. Case V, with a positive blood-culture of Brucella melitensis, is particularly interesting because of the fact that the positive agglutination appeared after the injection of milk. We

have no means of knowing whether this patient has an arthritic type of undulant fever or whether a Brucella melitensis infection was introduced by the milk injections

CONCLUSION

The 5 cases of Brucella melitensis reviewed indicate that undulant fever occurs in persons living in large cities Tests, therefore, for Brucella melitensis should be made in all low-grade fevers of an abscure nature

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PATHOLOGIC CONFERENCE OF DRS RICHARD H JAFFÉ AND RICHARD A LIFVENDAHL

COOK COUNTY HOSPITAL

ATROPHIC CIRRHOSIS OF THE LIVER ASSOCIATED WITH MARKED ENLARGEMENT OF THE SPLEEN AND A LIVER-CELL CARCINOMA

DR RICHARD A LIFVENDAHL This was a man, fifty six years of age, who was in the hospital for a short period He was sent in with a diagnosis of cirrhosis of the liver He said he had been in good health until five months before entrance, when he noticed a slight fulness of the abdomen after meals Three months before entrance he noticed the onset of an abdominal swelling which was progressive in character In addition, he had a slight amount of pain in the right upper quadrant which had been present for two weeks before his entrance He also had marked loss of appetite for a period of three weeks Stationary type of jaundice had been present for fifteen days Some constipation and the passage of two clay colored stools had been noted for a period of two months Only on two occasions did he vomit any material which was regarded as being bile Over this period he lost 30 pounds in weight He had some palpitation of the heart, particularly when the abdomen became swollen Associated with this there was a slight amount of pain in the lumbar region He also had some urinary retention, with moderate diminution in the amount of urine, coming on at the same time as the swelling in the abdomen He said he had taken a moderate amount of alcohol, but not excessive

Physically he was well nourished, with a yellow tinge to the skin Temperature, pulse, and respiration were normal, and blood pressure was 154/48 The cervical vessels were distinctly

pulsating The chest was emaciated and the left side lagged somewhat There was a diminution in resonance over the left chest and faint friction-rub in the left axilla A murmur was audible over both the aortic and mitral areas of the heart The pulse was not regarded as being of the typical water-hammer type Examination of the abdomen revealed the most outstanding changes It was distinctly distended and stood out in bold relief as compared with his emaciated chest There was flatness in the flanks, though the anterior portion of the abdomen was tympanitic The liver edge was felt at the umbilicus

It was rather difficult to come to any conclusion as to what the character of the tumor was because of the large amount of intra-abdominal fluid On neurologic examination it was found that the pupils reacted sluggishly to light and were slightly increased in size The Wassermann test was 2+, but spinal fluid Wassermann was negative

A diagnosis was made of mitral stenosis with aortic regurgitation, also the possibility of hepatic cirrhosis because of the marked distention of the abdomen and the moderate intake of alcohol over a long period of time Also carcinoma of the liver was considered The determination of the icterus index gave a reading of 20 The senior intern examined the patient, and his conclusions were that he had a carcinoma of the liver and hepatic cirrhosis He made a rectal examination to ascertain the possibility of a primary tumor with secondary metastases to the liver, but no new growths were found Because of a positvie Wassermann reaction the possibility of a luetic hepatitis was considered He noticed, in addition, that the left radial pulse was of greater intensity than the right Ophthalmoscopic examination of the fundus showed myopic fundi, with rather sclerotic vessels In order to come to an accurate conclusion as to the type of fluid an abdominal paracentesis was performed The fluid obtained was bloody in character, it was examined by the Wassermann test and found to be negative His conclusions, in view of the further findings, were that the patient had a carcinoma of the liver, which may have been primary in the gall-bladder or in the gastro-intestinal tract or in the pancreas The patient showed

a very severe anemia, a rather outstanding thing in view of the bloody fluid in the peritoneal cavity The red count was down to 810,000, though the hemoglobin was 50 per cent

So we have a patient well along in years, whose outstanding findings is a marked amount of abdominal swelling, with the possibility of an explanation of the entire process on a cardiac basis or the probability of a liver condition to explain the entire picture, the supposition of carcinoma of the liver or a primary cirrhosis was not settled, at least so far as the physical examination was concerned The patient was in poor condition and consequently the work up was not as complete as usual

DR RICHARD H JAFFÉ The external examination of this case revealed a very markedly emaciated patient with an intense icteric discoloration of the skin and sclerae The abdomen was much distended From the abdominal cavity much blood tinted fluid was removed Considerable numbers of soft blood-clots were found in this fluid The liver was very large and had pushed the diaphragm upward There was a compression atelectasis of both lower pulmonary lobes The liver weighs 4500 grams It is cirrhotic and contains a large tumor mass which on microscopic examination shows to be composed of atypical liver cells It is a primary liver-cell carcinoma or, as we call it, a hepatoma following cirrhosis of the liver This is a relatively common combination Ninety per cent of all primary liver-cell carcinomas are associated with atrophic cirrhosis In this case we can see all the different stages from plain cirrhosis to benign adenoma and finally a malignant tumor When you look at the cut surface it is a very colorful picture, almost like mosaic, some areas are yellowish brown, some bright yellow, some a deep olive green These yellowish-brown areas which show the fine network of connective tissue are the areas of atrophic cirrhosis Under the microscope we find islands of liver tissue separated by proliferated connected tissue In cirrhosis we always find atrophy and regeneration, and in this case the regeneration is very marked The yellow areas which are soft and slightly elevated are adenomas In these adenomas bile secretion is still going on and you find bile pigments in the liver cells and in the

bile capillaries between the liver cells Finally, there is this large area, soft throughout, which is carcinomatous In spite of the carcinomatous degeneration we still can recognize the type of cell as liver cell The cells are large and have relatively small nuclei They are arranged in irregular coils In these areas we do not find the intercellular bile capillaries This is important Sometimes the question comes up, is this an adenoma or is it a liver-cell carcinoma? There may be some bile formation in liver-cell carcinoma In carcinomatous areas you will never find intercellular bile capillaries We may find a similar structure in adenoma, but we never find these structures in carcinoma An early carcinoma may produce bile The liver cells pile up the bile There is no outlet for the pigment These nodules become a deep green These deep green areas are carcinomatous and stained by bile pigment The reddish-brown areas are carcinomatous nodules with regressive changes A large metastatic node on the lower surface became hemorrhagic, softened, and perforated into the abdominal cavity and caused the blood-stained content in the abdominal cavity We are dealing in this case with a hemorrhage into the abdominal cavity from a ruptured carcinomatous metastasis

Under the microscope there is a section of the liver tumor In the upper field you see the degenerating cells and in the lower half the carcinoma These tumors usually metastasize to the periportal lymph-glands

As an incidental finding there was a little polyp in the rectum Usually in atrophic cirrhosis of the liver we find a huge tumor of the spleen In this case the tumor weighed 900 grams, more than five times the normal weight This is evidence of the preceding cirrhosis because a primary carcinoma of the liver would hardly produce such a marked enlargement of the spleen

Then the patient had a syphilitic aortitis with very severe atheromatous changes In some places you can recognize a wrinkling of the intima Then you find calcified plaques The heart was slightly hypertrophic with secondary brown atrophy

In summarizing, this was a case of atrophic cirrhosis of the

liver, associated with a marked enlargement of the spleen The regenerative changes in the liver went beyond the physiologic limits to the formation of adenomas and finally to a liver-cell carcinoma A large metastasis became softened and broke into the abdominal cavity, giving rise to a considerable hemorrhage

DR HARRY SINGER This patient was tapped and blood withdrawn I thought some vessel had been entered in making the puncture We wondered at the time whether there was a softened metastasis to cause this bleeding It was surprising to see how much blood was withdrawn, and it looked as though the trocar had entered a vein

BACTERIAL THROMBO-ENDOCARDITIS IN A PATIENT WITH BEGINNING MYCOSIS FUNGOIDES

DR LIEVENDAHL This autopsy was performed on a patient who, for a period of eight days, was in one of the medical wards with a diagnosis of chronic bronchitis and suspected pulmonary tuberculosis

He was a white male, fifty four years of age, who had felt well until seven years ago, when he left work to take care of his invalid mother He became ill, lost his appetite, and over a period of three years his symptoms increased markedly With the death of his mother, two and a half years ago, there was a marked exacerbation of the symptoms and he was unable to return to work Occasionally, at intervals, it was necessary for him to be at work for a period of a week or two About one week before his entrance into the hospital he developed a burning pain in the right epigastric region which was slightly relieved by taking soda He had a diarrhea for a period of a week in which he passed five or six watery stools a day He attributed this to the fact that he had taken a bottle of citrate of magnesia before the onset of the diarrhea In addition, we found on going over his symptoms that his appetite had been poor, that he had been constipated for a period of twenty five years, he occasionally had palpitation of the heart, and on numerous occasions, particularly during the fall, he had nose bleed and night sweats As regards the genito-urinary symptoms, he had nocturia for several years, two or three times a night He had some tingling of the hands during the month previous to entrance In the past history the only thing was influenza two years ago

Physically, he was a poorly nourished white male, not acutely ill. Pulse, temperature, and respirations were normal Examination of the tongue showed it was rather smooth and the papillæ were rather atrophic. In the neck the cervical glands were four in number, rather small, but distinctly palpable

Examination of the chest showed an emphysematous type of thorax There was a diminution in resonancy and breath-sound over the apices Examination of the heart revealed a systolic murmur at the apex There was some abdominal rigidity which made it difficult to palpate the underlying organs The liver margin was palpated one finger below the costal margin On examination of the scrotum it was found that the testicles were enlarged to three times normal size The skin showed a brown pigmentation over the entire trunk Associated with this, there were many verrucous lesions, elevated patches, and scaling patches over both hands and legs The scales which were present were removed with relative ease Associated with these lesions were many discrete, red, pin-head-size blebs over the trunk and extremities In the axillæ and in the inguinal region there were some enlarged glands which were not attached to the skin

With this history and findings the question was raised by the junior intern as to whether we were dealing with a Hodgkin disease, but partly because of the atrophic papillæ and smoothness of the tongue, also the possibility of pernicious anemia The skin condition was regarded as a chronic eczema Because of the findings in the chest a chronic tuberculosis associated with pulmonary emphysema was also considered

The senior intern examined the patient after this and obtained a few facts in addition The glands that were palpated had been present for a period of five years In addition, he palpated the posterior cervical group, the epitrochlear, and the axillary group, also under the skin of the chest there were enlarged glands The pigmentation had been present for ten years and the hyperkeratotic thickening had been present for a period of thirty-five years His diagnosis was Hodgkin's disease, with the possibility of a myelogenous leukemia, and a carcinomatosis of the skin

On the day of his death the patient became suddenly very dyspneic and cyanotic His head was deviated slightly to the right and the jugular vein on the left side was thought to be bulging This was associated with swelling of the right side of the chest and axilla The heart tones, on examination at this

time, were found to be very weak with a "crackling sound" over the precordial region

Because of the possibility of blood dyscrasia blood examination was made, which showed 75 per cent hemoglobin, 4,500,000 red cells, 38,000 leukocytes, with 80 per cent polymorphonuclears, and 18 per cent eosinophilic leukocytes In addition, further work up showed creatinin 3 7 and urea nitrogen 149 mg per 100 c c. of blood

Roentgenologic examination of the chest showed a healthy chest

So, for over a long period of time, this man had had symptoms referable to the skin, a progressive weakness over this period, suddenly developing epigastric burning sensation, and diarrhea, and in addition to the symptoms referable to the heart and gastrointestinal tract, also some referable to the nervous system, particularly shortly before his death, deviation of the head to the right, with the sudden development of cyanosis The patient died suddenly as compared to his previous condition while in the hospital.

DR. JAFFÉ On the autopsy table the pigmentation of the skin was quite distinct There was a diffuse thickening of the skin of both arms, with peculiar deep brown, crusted lesions After removal of these crusts the smooth, normal skin of the arm was exposed Similar changes were found on the lower extremities Then there was a diffuse swelling of the left side of the neck. Of the internal findings the outstanding feature was the changes of a very severe septic condition The blood showed hemolysis There was a hemorrhagic discoloration of the internal organs, most marked in the intima of the aorta Accompanying these swellings on the side of the neck there was a diffuse, inflammatory edema of the connective tissue of the neck There was a diffuse edema of the soft palate, marked swelling of both tonsils, and in the left tonsil there was an ulcerated area 1 x 1.5 cm in diameter Then, as mentioned in the clinical history, there was a diffuse lymph adenopathy which led to the first diagnosis of Hodgkin's disease The lymph glands about the aorta and hilus of the spleen formed large masses, and in

these masses we were still able to distinguish the single lymph glands

I will show you first the peripancreatic lymph-glands The lymph-glands are very large, but it is not the macroscopic picture of a Hodgkin lymphogranuloma, it also is not the picture of a leukemia The glands are soft, indeed very soft, and of a purplish-gray color In Hodgkin's disease the glands are rather firm and rubber-like in consistency, and the color is a definite light yellow There are usually areas of whitish fibrosis and small opaque areas of necrosis Here the glands are decidedly swollen, soft, and markedly hyperemic, of a deep purple gray color In the lung we found several small elevated areas Then the liver, too, was enlarged, weighing 1960 grams, and the areas around the branches of the portal vein stood out very distinctly There was a fibrosis of the periportal connective tissue If you will look quite close you will see many little nodules, pin-head sized, of reddish-gray color, and in the center of these nodules is a little opening These are the smallest branches of the portal vein The kidney showed a markedly septic cloudy swelling There was cloudy swelling also of the liver parenchyma

The last pan contains the aorta, showing the diffuse hemorrhagic discoloration of the intima The heart is hypertrophic, weighing 400 grams The pericardial sac is rather firmly adherent to the heart It was quite difficult to separate it The myocardium is deep brown in color and friable The cusps of the mitral and aortic valves are covered by light yellow thrombi The thrombi are rather small, soft, adherent, and composed chiefly of fibrin There is slight fibrotic thickening of the free margin of both mitral and aortic valves, suggesting that the patient had a mild rheumatic endocarditis perhaps years ago The thickened valves are covered by soft, yellowish-gray thrombotic masses It is most likely that on the basis of a preceding rheumatic endocarditis, an acute bacterial endocarditis has developed The outstanding feature is undoubtedly a septic malignant thrombo-endocarditis

Hodgkin's disease was mentioned in the beginning I excluded it just from the macroscopic appearance The spleen

was small The blood showed 18 per cent eosinophils There was also a marked eosinophilia in the internal organs A lymph-gland was removed at the biopsy and was found to he infiltrated by an enormous number of eosinophilic leukocytes The nodular infiltration in the liver and the increase of the peri-portal connective tissue were due to the enormous accumulation of eosinophilic leukocytes In the spleen were a large number of eosinophil leukocytes Eosinophilia in bacterial endocarditis is uncommon In acute septic conditions the eosinophils usu ally disappear The appearance of eosinophils in the peripheral blood is usually accepted as a sign of recovery

The patient had these peculiar lesions of the skin for over thirty years They came on in the spring and fall, like an allergic or anaphylactic condition In these allergic diseases of the skin and in chronic eczema eosinophilia is very common When we take the bone marrow in a case of long standing eosinophilia we find that it is composed chiefly of eosinophilic granulocytes So, when a man with an eosinophilic bone marrow, due to a pre existing allergic condition, develops a severe septic condition, his response will be an eosinophilic one I feel that everything can be linked into the picture of bacterial endo-carditis, that the infiltration of the liver and the swelling in the lymph glands are due to a septic condition with endocarditis There is only one condition that has to he excluded, and that is mycosis fungoides In mycosis fungoides we have first the stage of generalized eczema, and this gradually passes into the stage of granulomatous lesions in the skin, and sometimes in very rare instances in the internal organs The eczema is the first stage of mycosis fungoides and may go on for many, many years There are a few cases on record in which the eczema stage of the skin was followed and complicated by a granuloma tous condition in the internal organs In mycosis fungoides eosinophilia is very characteristic. We may get 60 to 80 per cent eosinophils So in the differential diagnosis, if we get a generalized lymphadenopathy in a case of long standing eczema, with very marked eosinophilia, we have to consider the possibility of mycosis fungoides For the time being I feel it is more logical

to make a diagnosis of a bacterial thrombo-endocarditis in an individual whose myelopoietic system has been altered by a pre-existing, long-standing allergic condition of the skin

DR J G CARR Do you mean that the glands were enlarged over a period of four years as a result of the skin disease and that the bacterial endocarditis was a terminal affair?

DR JAFFÉ The glands were enlarged as a result of the skin lesions, but the enlargement increased during the last period of his illness

DR CARR How do you account for the tremendous cyanosis? We thought it might have been a very severe infection in a man who was already in a condition of markedly lowered resistance The infection seemed to spread not from the throat to the neck, but rather from a wound in the arm where the gland was taken out It was over the chest and axilla when I first saw him I saw him thirty minutes before his death and he was very badly cyanosed He made one think of a severe respiratory obstruction He did not have edema and we wondered if he had a ruptured aneurysm with a hemopericardium We also took into consideration the possibility that he had a very severe purulent infection following a minor surgical operation It seemed to me if he died of infection that it was probably an infection from the skin because it started on the arm

DR JAFFÉ This is a very interesting question, especially the question of severe cyanosis The lung showed very marked congestion The capillaries were blocked by agglutinated erythrocytes I must direct your attention in this case to the severe alteration of the red cells The degenerated blood-cells may block the pulmonary capillaries, so causing the cyanosis

DR CARR The explanation you give about the cyanosis is very good We thought of multiple emboli It came on within twenty-four hours, in the last hours before death When I saw him he was blue all over

DR JAFFÉ In experiments with hemotoxins one finds very marked cyanosis The hemotoxins of bacterial origin destroy the red cells The microscopic picture of the lung supported this explanation

PARENCHYMATOUS GOITER WITH A PERSISTENT THYMUS AND HYPERPLASIA OF THE LYMPH-GLANDS

DR LIEVENDAHL THIS is a white man, fifty years of age, who was in the hospital for only four days He was sent up with a diagnosis of exophthalmic goiter He said he was well until a year and a half ago, when he experienced weakness The weakness progressed so markedly that he was unable to lift any object, and he felt as though his legs would give way under him He was unable to do any work for a period of fifteen months Nervousness and marked tremor were present His speech was very rapid and also very thick In addition, he had occasional epigastric cramps and diarrhea at the onset of the illness, one and one half years ago He had lost a moderate amount of weight He had some palpitation, moderate dyspnea, and edema of the legs for one and one half years He also complained of dizziness which was accompanied with spots before the eyes

Physically, it was very apparent that he was extremely nervous and very restless However, he was described as not being acutely ill Temperature 98 8° F , pulse 130, and respiratory rate 34, blood pressure 192/80 The eyes were very prominent, there was a definite stare, and a distinct lagging of the upper lids The teeth were in very poor condition On examination there was found to be a large bulging mass in the region of the right lobe of the thyroid gland There was a definite bruit over this area and a well-defined pulsation

The chest was very emaciated Expansion was moderate There were very coarse respiratory sounds throughout both sides The left heart border was 10½ cm from midsternal line and the apex was in the fifth interspace and was distinctly pounding There was a presystolic murmur at the apex and a systolic murmur at the base.

The diagnosis was Toxic adenoma of the thyroid gland associated with exophthalmus and also aortic insufficiency The senior intern examined the patient, and in view of the pistol shot femorals and the definite capillary pulsation, he thought of arteriosclerosis, in addition His examination of the chest showed a diminution of breath sounds and, in addition, a bruit ing of the abdominal aorta There was definite tremor of the tongue and the palpebral fissures were very wide This diag nosis remained the same as the junior intern's, with the ad dition of arteriosclerosis

While in the ward his temperature rose to 103° F , and his pulse-rate to 136, and there were râles in the right lung In view of the chest findings and the temperature, the possibility of tuberculosis was taken into consideration

Summarizing the findings, we have a patient who presents the outstanding clinical manifestations of so-called typical exophthalmic goiter In addition, he has hypertension and then develops a terminal temperature of marked degree Whether the temperature was due to septic process or whether it is to be ascribed to the bronchopneumonia in the right lobe remains to be seen

DR JAFFÉ I will show you first the thyroid because our interest centers about this organ The macroscopic and micro-scopic examinations show a typical exophthalmic goiter From an anatomic standpoint we speak of parenchymatous goiter be-cause it feels like parenchyma The weight of the thyroid is 140 grams, whereas the normal weight in the region of the Great Lakes is between 25 and 35 grams

Both lobes are diffusely enlarged and there are no nodes The thyroid feels like a parenchymatous organ The color is a light reddish brown Sections of this thyroid are under the microscope and you can see the changes characteristic of ex-ophthalmic goiter The colloid is practically gone and is re-placed by a pale, thin, watery fluid The epithelium is hyper-trophic, highly cylindrical, and thrown up to papillary infoldings

We find so frequently in cases of exophthalmic goiter a per-sistent thymus This is also the case in the present observation,

the thymus weighing 12 grams and being composed of typical thymic parenchyma

This patient was fifty years of age Normally at this age we find the thymus consisting of fatty tissue with a few small islands of parenchyma and with a few Hassell's bodies As you know after puberty the thymus undergoes a physiologic involution, so that at the age of thirty five most of the thymus has been replaced by fat tissue We find this persistent thymus, which is important In disturbances in the glands of internal secretion we should not consider only one gland, because there is such an intimate relation between the different glands of internal secretion In exophthalmic goiter the changes are not restricted to the thyroid, we find characteristic changes also in the thymus, in the hypophysis, and in the other endocrine glands I show you the thymus to illustrate these relations

You heard from the clinical history that the patient's blood pressure was high, that he had aortic regurgitation, and that there was a marked difference between the systolic and diastolic blood pressure The heart is enlarged, 400 grams in weight, as compared to 300 grams for the normal heart Both ventricles, and especially the left, are thicker than normal The myocardium is firm and brownish red in color When I look at this heart I would say it is the picture of a hypertension heart There are no anatomic findings to explain the aortic regurgitation There are no changes in the aortic valves The question would arise as to whether there was some relation between the hypertrophy of the heart and the hyperplasia of the thyroid There are different attempts, especially in the older literature, to explain the hypertrophy of the heart and high blood pressure in exophthalmic goiter Some emphasize the compressions of the large vessels of the neck, thus interfering with the circulation of the blood Others emphasize the compression of the trachea I believe that the hypertrophy of the heart is the result of the hypertension What does it mean? The peripheral arteries, especially the arterioles, have an increased tonus from an improper relationship between stimulation of the vasoconstrictor nerves and vasodilatory nerves In hyperten-

sion there is overstimulation of the vasoconstrictors and, therefore, there is an increased resistance to the blood flow The heart compensates in order to overcome the peripheral resistance and thus becomes hypertrophic We know in exophthalmic goiter there is an abnormal irritability of the autonomic nervous system We are not surprised to find in this condition an overstimulation of the vasoconstrictor nerves, just the same findings as we get in essential hypertension

Of the other findings in this case I mention the hyperplasia of the lymphatic tissue When we make a differential blood count in exophthalmic goiter we usually find a lymphocytosis The spleen weighed 250 grams and was rather soft

This softening of the spleen was due to the complicating bronchopneumonia The patient died finally from confluent bronchopneumonia involving the posterior parts of the lower lobes

In summarizing in exophthalmic goiter we find on the autopsy table a parenchymatous goiter, with or without nodular hyperplasia, a persistent thymus, and hyperplasia of the lymph-glands We also find hypertrophied heart which results from hypertension One thing we cannot explain on an anatomic basis is this aortic regurgitation There was no insufficiency of the aortic valves and no abnormal widening of the aortic arch

DR LIFVENDAHL Because of the patient's rather serious condition it was impossible to obtain a basal metabolism rate

CLINIC OF DR JESSE R GERSTLEY

NORTHWESTERN UNIVERSITY MEDICAL SCHOOL

APPENDICITIS IN CHILDREN

Case I.—This fifteen year-old girl was taken acutely ill about 10 o clock last night with severe abdominal pain nausea, vomiting extreme prostration and high temperature She is really an adult, but in the excitement was admitted to the Children s Hospital on account of her small stature Her chief complaint was of excruciating abdominal pain mostly on the right side and extending around to the back. A severe headache complicated the picture and made her conversatioo incoherent The physician called in the emergency made a leukocyte couot, finding 16 000 with a differential of 80 per cent polynuclears Inasmuch as her urine was negative and in view of the painful, tender abdomen and the blood findings he diagnosed acute appendicitis and rushed her to the hospital

Fortunately the child was admitted by an intern who had a good knowledge of medical diagnosis. The physical findings were as you see them now Notice the position of the child she lies oo her side the head is drawn acutely backward the legs are drawn up She seems unconscious. There is a convergent strabismus and the pupils react only slowly to light. It is not necessary to elaborate at much greater detail By this time you have suspected the diagnosis A lumbar puncture made last evening confirmed the suspicion of acute epidemic meningitis.

Here then we have a girl who was taken ill with acute meningitis and in whom the root pains radiating from the spinal segments gave many of the symptoms of acute appendicitis

Case II.—These organs are those of a six year-old girl When I was called to see her she had had a slight stomach ache for a few days I found a child apparently not acutely ill nor even uncomfortable. Her temperature was 99 F her leukocyte count 6000 the differential absolutely normal. In view of the *history* and of the very slight rigidity and tenderness in the right lower quadrant I thought it safer to call surgical consultation One of the *city's* leading surgeons examined the abdomen and in view of the vague findings was not certain as to the procedure We decided however that it might be safer to open the abdomen The operation showed a ruptured gangrenous appendix with some free pus in the peritoneal cavity The child died in a few days from general peritonitis.

These 2 cases tell the whole story of appendicitis Finney cleverly sums up the whole situation as follows "In adults the tendency is to mistake something else for appendicitis In children one mistakes appendicitis for something else"

A concise presentation of the subject of appendicitis in children is very difficult, for

1 The symptoms are extremely variable

2 The progress of the disease is rapid The child may have a catarrhal appendix one day and a ruptured appendix the next, *i e*, the symptoms depend upon the day the patient is seen

3 Symptoms of appendicitis and peritonitis are often combined

4 The ruptured appendix presents a symptom complex of its own

5 Pediatricians see innumerable cases in which the diagnosis of appendicitis is more or less questionable

(*a*) Nasopharyngitis with intestinal fermentation
(*b*) Nasopharyngitis with appendicitis
(*c*) Recurrent navel colic
(*d*) Cyclic vomiting

Mortality—In the United States birth registration area for the year 1922, in children under five years, appendicitis caused 516 deaths, meningococcus meningitis 477, septic meningitis 466, tetanus 452, and acute poliomyelitis 428 From intestinal obstruction there were 1485 deaths, but probably some of these should have been included under appendicitis

Putting it differently, 4 per cent of all deaths from appendicitis occur during the first five years, while only 2 per cent of all cases develop at that time So we see that the mortality in children under five years is exceptionally high

Frequency—Appendicitis is the most common surgical disease of young children Sixty per cent of all laparotomies in children are for appendicitis, and ninety-five per cent of all cases of peritonitis

This statement is confirmed by international statistics The Dublin Children's Hospital, in 100 consecutive laparotomies reports 37 for appendicitis, 19 for tuberculous peritonitis, and

17 for intussusception The Evanston Hospital Chicago, during a five year period, reports 8 appendicitis cases and 6 intussusceptions in children under three years, and 18 appendicitis cases and 6 intussusceptions under five years

Occurrence in Infants —Although appendicitis is most frequent in children over five years it is not unknown to infants Deiss reports 1 case under six months, 1 case from six to twelve months (466 admissions), 12 cases from one to three years (1570 admissions), 11 cases from three to five years (1090 admissions), and 40 cases from five to ten years (1593 admissions)

Prenatal appendicitis has been described by Hill and Mason On delivery the baby's abdomen was markedly distended He vomited severely the first day, though the temperature was normal The second day distention and vomiting were extreme and the temperature reached 102° F Death occurred on the third day The peritoneal cavity contained 130 c c of straw colored fluid The appendix was 2 inches long, was dark and swollen, and showed a perforation ½ inch from the cecum In 1901 Griffith reported a case in a three month-old infant Lannay diagnosed appendicitis in a baby of twenty-eight days, Buford in one of eight months, and Glonninger operated one at forty-one hours

In 1917 Abt reported a case in a nine month-old infant and collected 79 cases from the literature Twenty of these were under three months, 8 being associated with strangulated hernia In the group of three to six months there were 6 cases From six to twelve months, 11 cases, one to two years, 40 In a recent series of 42 cases at Sarah Morris Hospital for Children, Freedman reports two inflamed appendices in infants under two years of age

Anatomy —The cecum lies under the liver until birth Some say it does not complete its descent until about four months others say it does at birth In some cases it does not descend at all In general, the cecum of the child lies higher than that of the adult

The appendix lies free in the abdominal cavity and may point in any direction, often downward toward the bladder or toward

the ovary or curving backward behind the cecum The local symptoms during an attack depend on its location

The child's appendix is relatively larger in length and diameter and even approximates in absolute size that of the adult Compared to the length of the large intestine, it is 1 20 in the child and 1 40 in the adult The average length of five years is 7 6 cm , and at twenty to thirty years is 9 5 cm It has a funnel-shaped opening and a relatively larger aperture and so empties more easily than that of the adult

The coats of the organ are thinner than in the adult This has great clinical significance which will be discussed later

Histology—In the full-term fetus there is no lymphoid tissue During the first two weeks two to three lymph follicles and lymphoid tissue appear in the mucosa In a month lymph follicles increase to eight or twelve, and lymphoid tissue appears in the submucosa By thirty-two weeks the appendix appears as an actively functioning gland Whether the development of lymphoid tissue predisposes the organ to infection is a problem under discussion

Physiology—The vascularity of the organ is entirely out of proportion to its size Inasmuch as the glands secrete a glairy mucoid liquid possibly, in remote times, the appendix may have had to do with digestion

Pathology—Apparently the path of infection is by way of the mucosa The earliest attack shows suppurative foci in the mucosa and submucosa These extend rapidly through the coats Edema at the very beginning spreads quickly to the peritoneum

Finding of parasites, such as oxyuris, is more frequent than is usually thought

Symptoms—When called for the first time to a case of suspected appendicitis, the physician, after a routine history, inquires as to previous attacks It is well to remember that the younger the child, the less likely such a record Under five years, 6 per cent of children will report previous attacks, while under twelve years, 30 per cent of appendicitis cases give such a history

Appendicitis is twice as common in male children as in female

Classical Attack—The late John B Murphy, who did so much to clarify the whole subject, based his diagnosis on five cardinal points, occurring in the following order

1 Generalized abdominal distress
2 Nausea and vomiting developing within a few hours
3 Rigidity and tenderness in the right lower quadrant
4 Fever developing in a few hours
5 Leukocytosis

Symptoms in Children—While, in a general way, the symptoms in children follow Murphy's dictum, some or many may be absent, and in only the fewest cases do they follow the orderly sequence noted above

Pain—Unquestionably the cardinal symptom in children is pain Brown reported this in 98 per cent of his cases The pain is constant The child will not go to sleep and will not let anyone else go to sleep Due to the tension within the walls of the appendix, there is no period for relaxation as in gastro enteritis The child resents any change in position, and above all things will not sit up voluntarily and objects to being made to sit up But this pain does not follow the adult rules In 20 per cent of Richter's 208 cases in children, the general abdominal pain of the onset was absent In only 80 per cent was there pain in the right lower quadrant, and in 22 per cent of these this was the only pain complained of In 70 per cent of his cases pain localized in this region was present on the very first day The reason for the variability in pain symptoms will be discussed later

Vomiting—Nausea is almost invariably present and vomiting is usually repeated a few times during the first day It is a rather constant phenomenon, but is not persistent It occurs in about 80 per cent at the onset and is absent in the remaining 20 per cent In younger children the vomiting may be severe enough to suggest intestinal obstruction, but, as a rule, such a symptom does not develop without an associated peritonitis

Temperature—At the onset this may vary from 99° to 101° F Appendicitis rarely starts with a temperature of over 103° F

A higher temperature than this suggests the onset of some other ailment

Pulse rate is as important a symptom as the temperature It is elevated in all cases, but particularly so in toxic ones In the non-perforated it tends around 100 or less, and in the rup-ruptured appendices considerably higher

Leukocytosis —Careful examination will show an increase in the leukocyte count even before the fever A count of 10,000 is about a rough average for the onset of an attack, *but under no circumstances is the leukocyte count an index of the severity of the infection*

Constipation —This is a frequent symptom Diarrhea occurs only occasionally

Tympanites —This may occur in the catarrhal appendix, but is much more frequent when peritonitis sets in

Urination —Increased frequency and painful urination are not at all uncommon In such cases the inflamed appendix is often lying over the bladder

Physical Examination and Diagnosis —*Inspection* —The child lies quietly in bed and does not necessarily appear acutely ill He may be pale, and above all things he holds his abdomen quiet and breathes costally He may lie with his right leg flexed, or at any rate, he resents much manipulation of the right leg

The cardinal signs are those relating to the abdomen These are

(*a*) Involuntary muscular rigidity

(*b*) Local tenderness

(*a*) *Involuntary Muscular Rigidity* —As regards the involuntary rigidity, it is well to start palpation on the left side in order to gain the child's confidence Palpation should be light, as we are testing only muscular rigidity and not tenderness It is well to compare the rigidity of the right and left recti with one another and subsequently the muscles external to the recti with one another As these are softer than the recti, one should never compare such rigidity with that of the rectus on the same side, but only with the corresponding area on the other side Involuntary rigidity is present in fully 95 per cent of cases

(*b*) *Local tenderness* is an extremely valuable diagnostic sign It occurs when the inflammation has reached the peritoneum and thus is a great help in determining the location of the appendix. It is very hard to elicit in a young child, because he will cry at almost any manipulation of the abdomen I have found the following procedure to be of value Gain the child's confidence by examining the ankle The child will then automatically relax his abdominal muscles Then taking tight hold of the ankle, shake the body sufficiently so as to jar the abdomen The child often will place his hands over the sore spot in his abdomen, trying to steady it

In discussing local tenderness it is well to remember that the removal of the fingers may be even more painful than the direct pressure

In all doubtful cases a rectal examination should not be omitted Needless to say, this is particularly indicated where a retrocecal appendix is suspected

Variability of Symptoms—The great variability of the symptoms in infancy and childhood are to be explained by

1 An understanding of the innervation of the appendix

2 A recognition of the course of the disease

The appendix is innervated by the abdominal sympathetic The first effect of inflammation is to irritate this nerve, which in turn transmits its influences to the spinal nerves of the same segment Hence the first pain is in the umbilical region and the skin innervated by these spinal nerves Then, later, as the peritoneum becomes inflamed, the pain becomes localized to that spot of local peritonitis

The course in children is characterized by

(*a*) The insidious onset

(*b*) The rapid progress to gangrene and perforation

As regards the frequency of gangrene, Richter's series is striking

54	simple catarrhal
29	gangrenous, no perforation
26	gangrenous, perforation, no abscess
40	perforation, with abscess or peritonitis

Seeger, in 61 cases in children, reported 36 as ruptured, and of these, 38 per cent ruptured within forty-eight hours At Sarah Morris Hospital, Chicago, Freedman reports purulent appendices in 18 of 42 recent cases At the same hospital Bernard Portis operated 85 cases under twelve years of age, 36 of which were of the purulent type

The thinness of the appendix wall in children probably is a factor in the speedy progress of the disease, and thus it becomes clear as to why the symptoms of the initial catarrhal appendix become so rapidly fused with those of associated peritonitis

Differential Diagnosis—The onset of appendicitis must be differentiated from the prodromes of all acute infections It is well known that typhoid, measles, and in extreme cases, even pericarditis have been mistaken and operated on for appendicitis Of the infections, pneumonia is the one most frequently confused, and while cases of pneumonia are occasionally operated on for appendicitis, in infants appendicitis may be diagnosed as pneumonia In infants the latter mistake is particularly likely, due to the frequency of respiratory complications in infancy and to the fact that appendicitis may be ushered in by a slight respiratory infection

Other conditions frequently confused are gastro-intestinal colic, pyelitis, intussusception, inflamed Meckel's diverticulum, and peritonitis from other causes

Surgeons make the startling statement that every acute condition in childhood should be considered appendicitis until proved otherwise, and some even go so far as to say they would rather operate on a pneumonia by mistake than slip up on a ruptured appendix

Ruptured Appendix—There is no complication in medicine more misleading, more dramatic than that of a ruptured appendix in a child From a period of discomfort, malaise, and fever the child shows sudden improvement Pain diminishes Temperature drops to normal Leukocytosis disappears The child is well The appendix has ruptured, and for a few hours, during the period of relieved tension, there are no symptoms, and then, with a rush, comes the fatal peritonitis

In few conditions in practice does the physician so hold the life of his patient in his hands In few conditions is a mistake so fatal The physician called for the first time during such a period can so easily delay the operation that gives the only chance of life to his little patient. An adult would have consulted the physician hours or days before The child's illness is often overlooked until the fatal complication

If called for the first time at such a period I know of no sure method of diagnosis One must rely largely on a careful history If the child has had abdominal pain and fever which has *suddenly* been relieved, the physician must at once be on his guard He should never neglect to see this patient again within a few hours, nor should he be far from the telephone

Special Problems of the Pediatrician —The modern pediatrician attempts to see the baby shortly after it is born and at frequent intervals during early childhood During this time he often sees the child with mild ailments, for which some years ago he would not have been called While fully cognizant and appreciative of all that the surgeons have contributed he still sees many cases of abdominal pain in which the diagnosis is not clear It must be remembered that the surgeon is not called until the diagnosis is at least highly suggestive and surgical statistics are based on this type of case With our newer knowledge of appendicitis the pediatrician must ask himself whether these mild cases are or are not transient appendiceal attacks To illustrate, let me enumerate three or four such problems

1 As far back as 1909 Farssac (These, Bordeaux, 1909) emphasized the relationship between nasopharyngitis and appendicitis This has been observed by innumerable pediatricians ever since. With our newer knowledge of infections of the nose and throat pediatricians have learned that nasopharyngitis and kindred infections cause indigestion and intestinal fermentation The perplexing problem then, and one which is often impossible to solve in an infant, is

(*a*) Is this abdominal pain due to nasopharyngitis and intestinal colic?

(*b*) Is it due to nasopharyngitis and appendicitis?

(*c*) Is it due to both?

2 A symptom complex, described mainly by the Germans is that of recurring navel colic A child in perfect health is seized with colicky pains around the navel which last a few minutes to an hour and then disappear for weeks or months, to recur No other signs are noticed Theories vary from intestinal colic to neurosis One observer claims to have cured such cases by suggestive treatment, such as binding a coin over the navel In view of our newer knowledge of the innervation of the appendix, one wonders whether these may be most transient appendiceal attacks

3 Cyclic vomiting and acidosis have been considered as due to metabolic disturbance There is much evidence to suggest that some of these patients are relieved by appendectomy

I know of no way to answer the above questions except by further observation If all practitioners should keep a record of their patients during these attacks, and if such patients should later be operated on for appendicitis, examination of the appendix might show a previous inflammation There is need for much work along these lines

Treatment —The main treatment is, of course, surgical The medical treatment consists in not what to do but what *not to do* Besides keen observation and highly restricted diet the physician must be insistant on barring cathartics In Brown's 700 cases 111, or 19 per cent , were ruptured, but of the 73 who had received cathartics, 46, *i e* , 63 per cent , were ruptured

Appendicitis in its most virulent form is often caused by medical treatment The disease rarely goes on to an acute, spreading peritonitis unless purgatives are given Without these a localized abscess would probably be formed Brown is so insistent on these points that he says if a surgeon hears that physic has been given, he should operate, no matter what the symptoms may be

SUMMARY

1 Appendicitis occurs more frequently in children than is generally considered

2 The onset is insidious, the symptoms variable, the course extremely rapid *Pain* is the cardinal symptom

3 Rupture may occur within forty-eight hours

4 The ruptured appendix with its sudden cessation of all symptoms is one of the most dangerous and fatal pitfalls of pediatrics

5 In young children with any sort of abdominal symptoms appendicitis should always be suspected until ruled out

6 There still remains considerable work to be done in cases of transient abdominal pain occurring in apparently well children

CLINIC OF DR WILLIAM A BRAMS

Cook County Hospital

HEART FAILURE

Today's clinic will be devoted to a discussion of heart failure Generally speaking, heart failure may be divided into that affecting the left side and that in which the right side of the heart gives way functionally Such a division is advisable because the symptoms of one are quite different from those of the other and because the prognosis and treatment are different in the two varieties

It must be mentioned in passing that heart failure in today's discussion refers chiefly to failure of the ventricles Failure of the auricles does not produce the symptoms to be described and many patients go about their business in comparatively good health when the auricles are not functioning well, as in cases of chronic fibrillation Bearing in mind these preliminary remarks, let us briefly mention the more important manifestations of the two forms of heart failure

The phenomena of importance which are observed in left heart failure are

Attacks of cardiac asthma, particularly at night

Cheyne Stokes breathing

Acute pulmonary edema

Cough, often nocturnal and very resistent to ordinary treatment

The chief signs are râles in the lungs, dyspnea, and signs of the causative factor, such as of hypertension, luetic aortitis, chronic nephritis, arteriosclerosis, etc. Note that edema, cyanosis, venous engorgement, and large tender liver are not mentioned

The important manifestations of right heart failure are quite different, in fact, they are the very ones which were mentioned as being absent in left heart failure These are

Pain and tenderness in the liver region and enlargement of this organ These may be the very first signs of this type of heart failure, long before edema or marked dyspnea occur

Edema and effusion in the serous sacs

Venous engorgement

Cyanosis

Oliguria

We shall now present two patients, each of whom is a fairly typical example of the forms of heart failure which are to be described

Case I —This patient, a laborer forty-two years of age, was in good health until seven months ago, when he noticed that he was getting short of breath on exertion *He had never experienced such a symptom before* The shortness of breath increased rapidly in severity until he was obliged to go to bed At first a measure of relief was obtained, but soon a number of pillows were required to keep the patient propped up in bed Even this procedure proved inadequate at night and eventually *attacks of shortness of breath lasting about a half hour* disturbed the patient's sleep The *sputum was foamy and blood streaked* during some of these attacks of nocturnal dyspnea There was no pain in the abdomen and the ankles were not swollen as far as the patient could remember These symptoms forced the patient to enter a hospital, where he remained for a few weeks His improvement did not last long, and he was again obliged to go to a hospital in spite of the fact that he continued to take the medicine which his doctor prescribed for him

You see before you a muscular man who, in spite of his splendid physique, is very dyspneic Yet, in spite of his marked dyspnea, there is no gross edema or evidence of ascites There is a disproportion of the usual evidences of cardiac failure Let us examine this patient a little closer, as the history and signs are quite typical of the type of heart failure from which he suffers. The pupils are a little sluggish to light, the carotids are hopping, and the pulse at the wrist is of the water-hammer variety These few findings are very suggestive not only of the underlying pathology but also of the cause

The apex-beat is circumscribed, but heaving in character, and is definitely displaced downward and to the left Percussion reveals a so-called aortic type of cardiac dulness in which the enlargement is chiefly downward and to the left, while the upper half of the left border is either straight or concave The dulness at the upper part of the sternum is definitely increased in width, and percussion along the length of the sternum shows that the upper half is dull while the lower half is resonant. A double murmur is heard over the entire precordium, but is loudest at the aortic area and sounds almost like a

buzz saw A few scattered râles are found in the base of the right lung The veins of the neck are not distended there is no edema or evidence of ascites and the liver is neither palpable nor tender The blood pressure is 160 systolic and 20 diastolic. The knee-jerks are reduced

The diagnosis is obvious, we are dealing with a case of luetic heart disease with luetic aortitis and aortic insufficiency It is interesting to consider the underlying pathology in order to gain a correct idea as to how these anatomic changes play a part in the production of the signs and symptoms of this condition The luetic process in the aorta first attacks the adventitia of the ascending arch, beginning as an endarteritis of the vasa vasora, which nourish the aortic wall itself There is also a perivascular infiltrate around these vasa vasora This results in an interference with the blood supply to the aortic wall, particularly to the media which, in turn, undergoes degeneration as a result of the diminished blood supply It is possible that the luetic toxin exerts a direct effect on the aorta in addition to the foregoing The media normally contains very many elastic fibers and it is this element which gives the aorta that quality of elasticity and resiliency which enables the vessel to withstand the shock during each systole of the heart The normal aorta, by virtue of these properties, can give when the blood is forced into it by the heart, and again resumes its former condition during diastole We have seen that the media undergoes degeneration in lues and that disappearance of the elastic fibers is a very prominent feature in this change The lost elastica is partly replaced by connective tissue which is unyielding for a while The constant systolic action of the heart distends the now inelastic aorta and the connective tissue begins to stretch, but the elastic action of the normal layer is missing, with the result that the vessel remains dilated and flabby We now see why the aorta becomes wide in lues and why widening of the aortic area on percussion or *x* ray is a very important sign of this condition The process in the usual form of luetic aortitis is generally diffuse so that there is a generalized widening of the aortic area Aneurysm occurs if the same process is localized, so that a circumscribed pouching results from the same cause

The aortic insufficiency in lues is explained on the basis of the changes occurring in the aortic ring and in the aortic valves The luetic process involves the valves at their commissures near the attachment to the aortic wall The body of the cusps is not changed much The valves become adherent to the aortic wall at the commissure, so that the cusps cannot close with one another during diastole because of the shortening due to this adhesion It must be noted that the valves form no obstruction to the outflow of blood because of their attachment to the aortic wall, there is only an interference during attempted closure of the cusps It is now evident that aortic stenosis on an anatomic basis is not a part of luetic involvement in this region and that stenosis of the aortic orifice, if actually present, is a strong argument against syphilitic disease The picture is quite different from rheumatic involvement of the aortic valves where the valve margins are thickened and adherent to one another for a great distance along the margins, producing an actual narrowing of the aortic orifice Clinical experience teaches, therefore, that a double aortic lesion is either not luetic in nature or is complicated by some other factor, such as rheumatism

Our patient shows a systolic murmur at the aortic area and this finding needs explanation since it is not due to stenosis We have seen that the aorta is widened anatomically The blood passes the aortic orifice and, as it enters the widened vessel, the blood column spreads apart, so to speak, in order to accommodate itself to the increased space This causes a series of eddies which set up vibrations These vibrations are recognized by the ear as a systolic murmur because these changes occur during the expulsion of the blood from the heart It is important to remember that this or some other cause may produce a systolic murmur at the base of the heart without there being any actual stenosis of the aortic orifice

The symptoms are also of importance as they point to involvement of the left side of the heart, that is, they are significant of left heart failure The attacks of nocturnal dyspnea coming on during sleep and lasting for a short period of time are very suggestive The fact that the patient has at times expectorated

pinkish, frothy sputum during such attacks signifies that attacks of acute pulmonary edema, as well as of cardiac asthma, have occurred Both result from weakness of the left ventricle with pulmonary congestion and are often very alarming The picture is quite different in attacks of right heart failure in which venous engorgement, cyanosis, and large, tender liver are found The manner of onset in luetic heart disease is also rather suggestive The patients are usually of about middle age, well built, and have been in good health until the heart gives way in the manner described The onset is usually rather rapid and generally progressive There is not the history of a long standing heart affection with periods of complete remission alternating with attacks of decompensation as occurs in rheumatic heart disease. The latter are usually younger patients and have known of their condition for several years It is particularly *important to remember that we must suspect lues in a patient of about middle age who for no reason becomes decompensated and especially if there are evidences of aortic insufficiency* Our suspicion in this instance is confirmed by the finding of a positive Wassermann reaction, but it is also wise to remember that a negative result occurs in about one-third of all cardiovascular lues

The prognosis in luetic heart disease is not good These patients react to digitalis and rest at first, but these remedies ultimately lose their effect. Antiluetic treatment is of great value and relieves the symptoms in a striking manner, but the cure is more apparent than real It is difficult to conceive of an aorta being restored to normal when it has forever lost its elastic tissue and has become stretched and flabby Nor can the valves, which have become attached at the commissures, again become separated and function in a normal manner

Let us for a moment briefly review the important features of luetic heart disease as illustrated by this patient

The patient who has never before been short of breath becomes dyspneic for the first time in his life during middle age The symptoms are persistent and, although he has had short periods of improvement, the course is progressively downward

The symptoms of cardiac asthma coming on at night and

associated with occasional attacks of acute pulmonary edema, also at night, are suggestive of left heart failure

Clinical evidence of aortic insufficiency developing for the first time in a middle-aged man who has not had rheumatism, is highly suggestive of lues The diagnosis is finally established by the presence of widened aortic dulness, pupillary changes,and a positive Wassermann reaction

Case II —The next patient is thirty-four years old She states that she had an attack of rheumatism at the age of fifteen which kept her in bed for two weeks during which time her hands, knees, and wrists were involved She now complains of shortness of breath on ascending a flight of stairs pain in the abdomen, fulness after meals, and swelling of the ankles

Examination reveals moderate cyanosis of the lips and a purplish flush of the cheeks Let us first examine the abdomen because it is here that we gain much information as to the degree of cardiac decompensation present in this patient who knows that she has heart disease The liver edge is barely palpable, but there is distinct tenderness in the epigastrium and along the entire right costal arch There is no dulness in the flanks and the spleen is neither palpable nor tender

The *tenderness and pain in the liver region are due to acute stretching of the liver capsule and are very important early signs of failure of the right ventricle* This so-called right heart failure is very often ushered in by tenderness in the right hypochondrium and in the epigastrium, even before the liver is palpably enlarged The important liver signs which develop at a later date are objective and appear as the right heart failure progresses The liver then becomes palpably enlarged and the consistency is increased due at first to overfilling of the organ with venous blood and later to a deposit of connective tissue This firmness persists in chronic cases, but the pain disappears because the capsule is no longer acutely stretched An exacerbation at this stage will further engorge the large liver and cause acute stretching of the capsule with resulting pain We may thus surmise that tenderness alone in the right hypochondrium and epigastrium in a patient suffering from heart disease signifies early or recent acute right heart failure, a large, hard liver which is not tender probably means chronic right heart failure without recent exacerbation, while a large hard liver which is also tender speaks

for chronic right heart failure in which an acute exacerbation has recently occurred

The spleen in cases of right heart failure is enlarged anatomically as a result of passive congestion, but this enlargement is of moderate degree and not enough to make the spleen palpable In fact, a palpable spleen in cardiac failure speaks for complications such as infarct or superimposed bacterial endocarditis.

It should be mentioned in passing that oliguria is a very important sign of passive congestion of the kidneys, much more important and reliable than albuminuria

Let us now look for edema We find some at the ankles but it is wise to examine the sacral regions in bed patients because the edema in heart cases is static and tends to gravitate to the lowermost regions of the body depending upon the position of the patient Facial edema is very rare in these patients unless the patient sleeps with his head between his knees or when the edema is very extensive The edema, like the liver, is soft at first and later becomes more firm There are instances in which edema disappears in chronic cases, but ascites or pleural effusion persists This may be explained by assuming that prolonged congestion of these serous membranes causes a chronic irritation which results in persistent effusion due, rather, to low grade inflammation at this stage than to the causes which first produced edema and serous effusion This assumption is strengthened by the fact that the specific gravity of this fluid is slightly higher and that the albumin content is greater than in simple transudate

Further examination of the patient reveals that the apex beat is diffuse and weak with prominent pulsation in the epigastrium. The lower end of the sternum shows a slight heaving when the heel of the hand is pressed firmly in this region Percussion along the length of the sternum shows an increasing dulness as the lower half of this region is reached These signs speak for an enlarged right ventricle which is working harder than normally The area of cardiac dulness is more globular in shape than normally and extends considerably to the right of the right border of the sternum. The heart tones are weak, but no murmurs can be heard Neither the apex beat nor the borders of cardiac dulness shift as we turn the patient on the right or left side There

is no visible systolic indrawing of the apex, but the x-ray findings show a weakly contracting heart which is apparently firmly fixed in its pericardial sac

There is little doubt that we are dealing with a case of adhesive pericarditis following rheumatic fever and that right heart failure has now resulted as evidenced by the tender liver, edema, cyanosis, and reduction in urine output The prognosis of right heart failure in general is not hopeless and the results with digitalis are often striking Such improvement, if at all obtained in this instance, will be temporary, as the heart is working against a mechanical handicap, the adhesions to the pericardial sac, and to the neighboring structures which usually prove disastrous in a short time

CLINIC OF DRS JACOB MEYER AND DAVID H ROSENBERG

MICHAEL REESE HOSPITAL

"AGRANULOCYTOPENIA", "SEPSIS AGRANULOCYTICA" (AGRANULOCYTIC ANGINA)

THIS case is presented under the terms "agranulocytopenia" (David), "sepsis agranulocytica" (Feer) in order to emphasize our opinion that the so-called agranulocytic angina is not a distinct disease entity, but probably is a terminal reaction to either an overwhelming infection in a subject with low resistance or a constitutional disease

It may be well to recall that the symptom-complex of agranulocytic angina was first described by Schultz in 1922 The clinical characteristics were a stomatitis or angina in a middle aged woman occurring rather suddenly after a previous illness with fever, and terminating fatally in a period of a few days The blood changes are distinctive in the absolute reduction or complete disappearance of all granulocytes, polymorphonuclear neutrophils and eosinophils, from the circulating blood-stream The leukocyte count may be as low as 200 or less The lymphocytes are relatively increased and may be as high as 100 per cent There are no changes in the platelets and there is no hemorrhagic tendency Jaundice occurs in about 50 per cent of the cases The liver and spleen may be enlarged. The bone marrow shows an absence of neutrophils and eosinophilic leukocytes, and myelocytes

Since this observation many cases have been reported in the literature These case reports have served to emphasize the following facts

1 The symptom-complex may occur in children

2 There is no specific etiology, various organisms have been reported, such as diphtheria bacillus, Streptococcus viridans Bacillus pyocyaneus, and Vincent's spirochete and fusiform bacillus The disease has not been reproduced in animals

3 The angina or necrosis may occur on the mucous membrane of the mouth, gums, esophagus, stomach, duodenum, rectum and vagina, and even on the skin

4 A gangrenous bronchopneumonia may be associated

5 Anemia is not a part of the picture

6 Spleen and liver are often enlarged

7 Recovery occurs not only in children but in adults

8 Blood transfusions seem to give favorable results

Schultz called attention to the necessity of differentiating this condition from aleukemic leukemia, acute aplastic anemia and sepsis

Similar symptom-complexes have been described in endocarditis and in Hodgkin's disease The interest in this symptom-complex has stimulated many to believe that it represents a distinct disease entity of a specific etiology Others regard it as a malignant form of leukemia Still others regard it as a primary disturbance of the leukopoietic apparatus We are inclined to view it as a terminal reaction in a subject who has had a previous debilitating disease or overwhelming infection The case is, therefore, presented in detail

H L , a male, aged fifty-five, was admitted on July 1, 1929 His complaints were diarrhea, rapid loss of weight, tremors of the hands, fatigue and attacks of tightness over the chest

The patient was perfectly well until two and a half months before entrance, when frequency of stools, eight to ten daily, developed The stools were small, soft, light brown in color, with no blood or mucus His appetite was increasing, but a loss of weight was becoming apparent and progressing He had lost 57 pounds, his weight falling from 175 to 118 pounds Tremor of the hands and, at times, of the whole body, together with increasing "nervousness" (irritability, restlessness) and insomnia had been present since the onset of ill health Fatigue and shortness of breath were easily provoked, their development having been progressive The frequent bowel movements persisted, at times they were preceded by a cramp-like pain across the lower abdomen For two weeks he had noticed edema of the ankles which was worse on standing and at night, subsiding over night

About one week before admission while walking he was suddenly seized with severe pain across the upper sternum and chest constricting in charac ter This lasted from five to seven minutes during which time he walked up and down the bedroom. There was fear of impeoding death Similar at tacks recurred on three subsequent occasions within a period of ooe week, the last one occurring while sitting quietly in a chair He did not remember the character of the respiration

Further questioning revealed a history of epigastric distress of the na ture of pressure which was first noticed five weeks ago having no relation to meals.

Physical examiootion showed a temperature of 99 2 F pulse 84 res-pirations 20 He was a well-developed moderately emaciated white man, fifty five years of age who appeared rather pale but not acutely ill. No cough or cyanosis was present. Over the abdomeo the skin had ao edematous character There was evidence of loss of subcutaneous tissue Examination of the head and neck revealed prominent facial booes sunken eyeballs arcus senilis pale conjunctivæ mouth edentulous tonsils buried slight en largement of the right lobe and the right half of the isthmus of the thyroid the consistency of which was about normal

The epitrochlear axillary submaxillary and the postcervical glands were palpable but small

Examination of the chest showed it to be emphysematous. The move ment was symmetrical but mobility on the whole was restricted and there was marked supraclavicular retraction The lungs were hyperresonant breath sounds vesicular with slight increase in expiration No râles were heard. A diffuse apical pulsation was visible in the fifth interspace 10 cm. to the left of the midsternal line. Retromanubrial dolness was not increased. The tones were regular 84 in rate and somewhat soft The systole was partially replaced by a loud blowing systolic murmur heard most intensely at the apex and to the left of the sternal border but audible over the entire precordium The pulses were equal regular and synchronous tension not increased. The radials were palpably thickened Blood pressure was 134/66

The abdomen was slightly retracted soft with no evidence of ascites or tenderness. The liver edge was felt 2 cm. below the costal margin in the midclavicular line on deep inspiration This was smooth sharp not tender and of normal consistency The edge of the spleen was felt 1 to 2 cm below the costal margin This too was smooth sharp and of a normal consistency

There was slight edema of the feet and a marked coarse tremor of the hands, feet and sometimes of the entire body

Neurologic examination was normal except for slight hyperreflexia and tremor

Laboratory reports showed the urine to be negative. Examination of the blood gave the following findings hemoglobin 70 per ceot erythro-cytes 3,500 000 leukocytes 5600 polymorphonuclears 55 monocytes 10 basophils 2. Wassermann and Kahn tests were negative Blood-sugar 94 non-protein nitrogen 34 Basal metabolic rate was +23 7 Examination of the stools was negative

Tentative diagnosis Thyrotoxicosis chronic pulmonary emphysema

myocardial degeneration with moderate cardiac dilatation and early myocardial failure, arteriosclerosis, angina pectoris

The appearance of the patient suggested cardiovascular-renal disease. He was placed on a full diet, and given 1½ grains of luminal as indicated for insomnia

The following observations are of interest to emphasize the course in the development of the syndrome

July 4 More comfortable, polyphagia, pulse 74 to 78 at time of ward rounds, stools one to three daily, hard and well formed Ophthalmoscopic examination showed slight clouding of lenses Right Some haziness of disk outlines, physiologic cupping somewhat indistinct Fundus negative Vessels negative Left Right half of disk somewhat hazy with some indistinctness of cupping in this area, left half normal Fundus Slight increase in tortuosity of veins, otherwise negative Blood examination Erythrocytes 3,580,000, leukocytes 9300, hemoglobin 55 per cent , color index 78, polymorphonuclears 61, small lymphocytes 33, large lymphocytes 1, monocytes 4, basophils 1 Urine Amber color, specific gravity 1 018, alkaline reaction No albumin or sugar, occasional granular cast

July 7 Temperature 100 4° F this evening Dyspnea with tachycardia on exertion Stool cultures negative Basal metabolic rate repeated +43

July 8 Fractional Ewald 20 gm of lactose Free hydrochloric acid, 0 Total acidity 4°, 2°, 3°, 5°, 5° (achlorhydria)

July 10 Continued intermittent fever, maximum 101° F Pulse 80 to 96 Stool cultures negative No findings to explain fever x-Ray of gastrointestinal tract showed somewhat elongated and irregular pyloric antrum, otherwise negative Started on Lugol's, minims 15, twice daily for therapeutic test

July 11 Leukocytes 5800, polymorphonuclears 52, small lymphocytes 36, large lymphocytes 1, monocytes 7, eosinophils 2, basophils 2

July 12 Postcervical glands small and firm, inguinals firm Gastric analysis will be repeated using histamin to rule out functional achlorhydria. Temperature tonight 102° F , pulse 88 Comfortable Presence of enlarged spleen, palpable nodes in axillæ, neck, inguinal, and epitrochlear regions with fever suggests Hodgkin's disease in addition to hyperthyroidism, aleukemic leukemia to be considered x-Ray examination of lungs negative Heart diameter somewhat increased, but contour relatively normal Electrocardiographic studies Sinus rhythm, rate 70, P-R interval sixteen seconds, left axis deviation, occasional notching of P in leads 1 and 2, slurring of R in all leads

July 13 Temperature 102 2° F tonight, curve of remittent fever, minimum 100 6° Spleen seems larger and edge rounder Leukocyte count 2500 Has generalized patchy, erythematous rash over torso, upper and lower extremities Face flushed throat negative No Koplik's Small white spots on buccal mucosa, however Impression "Toxic rash"

July 14 All lymph glands larger Spleen larger, softer, and edge rounder White spots on buccal mucosa, not Koplik's General erythema of face and body Liver not larger Because of spleen and high basal metabolic rate must

consider some form of leukemia Temperature 102 8° F pulse 104 respirations 32 leukocytes 3500 polymorphonuclear neutrophils 41 transitionals 4 small lymphocytes 32 large lymphocytes 6 monocytes 11 Lymphoblasts and myeloblasts 4 1 lymphoblast 1 polymorphonuclear eosinophil 2 myelocytes. Platelets 350 000 Red blood-cells Signs of anemia. Complains of headache. Nothing else found

July 15 Temperature 100° to 102 4° F pulse 96 to 98 respirations 24 to 32. Face flushed. Spots on buccal mucosa persist yellow largest 1 mm in diameter slightly elevated, appearing opposite original sites of canine to first and second molar on either side nbove and below *Tonsils moderately enlarged* not hyperemic. Spleen enlarged further 5 cm. below costal margin Liver large, edge 4 cm. below costal margin in midclavicular line sharp, smooth firm not tender Blood examination Hemoglobin 55 per cent. erythrocytes 3,300 000 color index 0 83 leukocytes 1700 polymorphonuclear neutrophils 33 transitionals 10 small lymphocytes 33 large lymphocytes 8 monocytes 13 polymorphonuclear eosinophils 1 lymphoblasts 2 Platelets 255,000. Red blood cells show signs of anemia. Blood-cultures today negative. Widal negative. Bacillus abortus and B melitensis agglutination tests negative. *x* Ray of long bones and ribs negative

July 16 *Original complaint of weakness loss of weight and diarrhea when associated with findings of achlorhydria and anemia suggests possibility of malignancy it is possible that present blood picture might be due to some obscure malignant process It is conceivable that a primary anemia might terminate in this fashion It brings to mind again the possibility of some form of leukemia. It makes little difference whether we call it agranulocytosis or aleukemic leukemia but we are rather inclined to view this as a terminal agranulocytosis* Temperature tonight 101 8 F feels nervous Has lost 2 pounds since admission appetite very good Urine negative no Bence-Jones protein Leukocytes 1800 polymorphonuclears 22 transitionals 2 small lymphocytes 43 large lymphocytes 14 monocytes 11 eosinophils 5 lymphoblasts 3 Platelets 198 000 erythrocytes 3,300 000 hemoglobin 55 per cent. color index 0 83 blood pressure 114/58 started on digitalis minims 10 three times daily

July 18 Temperature 99 6 to 101 6 F pulse 72 to 98 respirations 20 to 30 Right postcervical lymph node excised Report by Dr Otto Saphir "The follicles are hyperplastic. The sinuses contain n large number of lymphoid and in addition show endothelial cells with very slightly stained vesicular nuclei. The architecture of the node is preserved The germinal centers seem somewhat smaller than normal There is no hemorrhage in the section Diagnosis Acute hyperplasia and hypertrophy of the lymph node. Leukocytes 3400 polymorphonuclears 40 small lymphocytes 41 large lymphocytes 6 transitionals 5 monocytes 8 platelets 220 000 Fragility test Complete 0.32 per cent. sodium chlorid partial hemolysis 0 44 per cent Clinical course unaltered since last note

July 19 Cyanosis of the nail beds and skin Spleen not enlarged any further Temperature rising further 103 F tonight pulse 72 respirations 24 appetite poor Leukocytes 3700 polymorphonuclears 61 small lymphocytes 7 large lymphocytes 11 transitionals 14 monocytes 7 erythrocytes 4 000 000 hemoglobin 40 per cent Urinalysis continues to be negative ex

cept for trace of albumin at times and occasional granular casts Bence-Jones protein negative No added findings to explain fever Lugol's discontinued

July 20 Leukocytes 1600, polymorphonuclear neutrophils 29, small lymphocytes 55, large lymphocytes 2, transitionals 6, eosinophils 1, monocytes 7, temperature 101 6° to 103 6° F , pulse 64 to 88, respirations 20 to 30, comfortable

July 21 Temperature 101 4° to 103 4° F , pulse 70 to 76, relative bradycardia noted, comfortable Leukocytes 2400, polymorphonuclear neutrophils 22, small lymphocytes 34, large lymphocytes 12, transitionals 15, polymorphonuclear eosinophils 3, monocytes 12, lymphoblasts 2

July 22 Spleen seems softer At present seems to fit in best with chronic lymphatic leukemia running an aleukemic course Temperature 104 2° F tonight, continues of remittent type, no complaints Leukocytes 2800, polymorphonuclear neutrophils 28, small lymphocytes 33, large lymphocytes 11, transitionals 16, polymorphonuclear eosinophils 1, monocytes 10, lymphoblasts 1, erythrocytes 4,000,000, hemoglobin 50 per cent , color index 0 63

July 24 Remittent fever persists, maximum 104° F *Complains of sore throat,* growing weaker, appetite poor *Pharynx and tonsils hyperemic,* considerable mucus on soft palate After removal, there was found on the *right tonsil a few pin-head spots* and a depressed area suggesting Vincent's angina Smear made and no Vincent's organisms found, but many diplococci Tongue dry, reddened, cracked, face flushed, brownish, maculopapular rash on abdomen and anterior chest Scleræ have subicteric tint Widal test negative, blood culture negative, urine shows more granular casts, stools negative, lost 4½ pounds since admission

July 25 Icteric hue to scleræ Pharynx injected

July 26 Icterus of scleræ increasing, suggestive icteric discoloration of the mucous membrane of the lower gum margin, spleen not as easily palpable, remittent fever continues, maximum 103 2° F , sore throat continues very weak, refusing meals, one involuntary stool Slight depression with gray, thin exudate in the left tonsil Hemoglobin 60 per cent , erythrocytes 3,700,000, color index 0 81, leukocytes 1600, polymorphonuclears 1, small lymphocytes 97, large lymphocytes 2 Blood drawn 8 to 10 hours later showed polymorphonuclears 2, small lymphocytes 64, large lymphocytes 23, transitionals 1, monocytes 3, 2 very early lymphocytes, 1 unknown mononuclear, 1 basket cell, 3 smudges, platelets normal in number but large Icterus index 63

July 27 400 c c blood transfused this morning Temperature rose to 104 8° F , pulse 112 to 116 Sore throat continues General condition becoming rapidly worse, more emaciated looking Little change in appearance after transfusion Considerable mucus on soft palate, fauces, and postpharyngeal wall Soft palate, fauces, and pharyngeal wall hyperemic, the two depressed areas on tonsils remain, thin gray exudate from the left tonsil, easily wiped off, leaving a red excavation Tongue dry, cracked Thin yellow nasal discharge since yesterday, nasal mucosa red Jaundice increasing, spleen somewhat smaller Occasional transitory râle at bases, faint *indistinct* systolic murmurs at the apex. Urinary output only 630 c c., taking very little fluids

July 28, 2 A. M Very dyspneic, respirations 40, diffuse erythema of the

torso with urticarial rash over extremities cheeks flushed pulse 116 fair quality voice weak. (Got out of bed)

8 A. M Acutely ill temperature 103 F, respirations 36 ood labored erythema faded replaced by definite icteric discoloration on lower extremities yellow urticarial rash red in some places over upper extremities and back there are red urticarial patches eyes and cheeks sunken increased jaundice Thick yellow-green mucus in fauces and on soft palate small gray patch in the upper pole of the left tonsillar fossa in previously described area throat otherwise same. Rhonchal fremitus over chest especially on the right side harsh breath sounds over right side anteriorly with many bubbling râles moist râles at bases liver palpable 1 cm below costal margin in mudclavicular line. Spleen 0.5 cm below costal margin not as round Bronchopneumonia of right side. Leukocytes 450 polymorphoouclears 0 small lymphocytes 86 large lymphocytes 9 transitionals 2 unknown monocytes 3 Hemoglobin 70 per cent erythrocytes 3 100 000 slight anisocytosis good color platelets 190 000 Sedimentation time twenty five minutes serum yellow Coagulation time three and one-half minutes blood sugar 127 noo protein nitrogen 83 creatinin 4 6 van den Bergh's test showed strong immediate direct reaction Urine Dark amber color specific gravity 1 015 acid reaction, albumin 1+ no sugar acetone, many granular and epithelial casts. Culture from throat Staphylococcus smear showed no Vincent s organisms.

11.30 A. M 250 c.c. of 8 per cent. glucose and 1 c.c. adrenalin given intravenously Expectorating large amounts of greenish mucoid sputum with rare blood streaks. Taking more fluids

12.30 P M Patient became cyanotic and dyspneic. Pulse 130 weak and thready respirations 46 Adrenalin administered and patient rallied

5.50 P M. Sudden cyanosis pulse 170 respirations 58 Patient died at 6.40 P M.

Final diagnosis Granulocytopenia, chronic atrophic pulmonary emphysema, myocardial hypertrophy (slight) with dilatation, chronic myocardial fibrosis with ventricular failure, ulcerative angina, arteriosclerosis, low grade chronic nephritis

July 28th *Pathologic Diagnosis by Dr Otto Saphir*—Acute ulcerative tonsillitis, bronchopneumonia of the right upper lobe, healed endocarditis (mitral and aortic valve), subacute splenic hyperplasia, acute fibrinous pleurisy of the right side, emphysema of the lungs, hypertrophy of the heart, the right side and moderate, generalized arteriosclerosis, coronary sclerosis, arteriosclerotic scars of kidneys, chronic passive hyperemia of the liver

External examination showed the body to be that of a well developed, somewhat undernourished, adult white male, about fifty five years of age Rigor mortis of the dependent parts had set in. The skin was bright yellow

Internal Examination A section of the skin showed decreased elasticity, subcutaneous tissue moist, and a decrease in subcutaneous fat

Pleural cavity In the right there was a small excessive amount of yellow liquid The surfaces corresponding to the upper lobe contained a large amount of fibrin

Pericardial and peritoneal cavities showed no abnormalities

There were several petechiæ in the subpleural and pericardial spaces

The heart was about the normal size and shape, the mural endocardium was smooth and glistening The margins of the mitral valve were thickened as well as the chordæ tendinæ which were fused by confluence The latter portions of the left and posterior leaflets of the aortic valve were adherent to each other in an area about 6 mm in length, this portion was very firm in consistency The myocardium, on cut section, was reddish in color and showed some increase of connective tissue The right ventricle was apparently somewhat hypertrophic and the wall was 4 to 5 cm in thickness

The elasticity of the aorta was somewhat decreased, while the upper portions of the thoracic aorta were practically smooth The lower and descending portions showed many yellow plaques of sclerosis, in addition to hyalinization and calcification

Both lungs were gray The midportion of the right upper lung was consolidated On cut section the latter was seen to be granular in appearance, reddish in color, and drier than the surrounding lung This extended for an area of 5×6.5 cm in diameter The remainder of the cut surface was gray-red and exuded, on pressure, a very excessive amount of grayish-red, frothy fluid

Both tonsils were somewhat larger than normal, the left showing an ulcerated area surrounded by marked hyperemia extending into the surrounding portions of the pharynx

The liver weighed 1400 gm , was about normal in size and shape, but somewhat firmer in consistency Cut sections showed markedly distended central zones which were reddish-blue in color, and many of which were fused by confluence, leaving

between them grayish periportal spaces showing marked increase of connective tissue The gall bladder was distended and filled with a thick liquid bile There were no stones present and the bile passages were patent.

The spleen weighed 340 gm and was enlarged and rather soft, and the capsule wrinkled On cut section the pulp seemed more abundant than normal The follicles were hardly visible and the trabeculæ were distinct.

The kidneys were normal in size and shape and the capsule stripped with ease There were several reddish scars throughout the surface Cut sections showed that the architecture was clear, boundary between the cortex and medulla were distinct, the medulla was very pale The pelves showed several petechiæ The bladder was distended with pronounced trabeculation

The middle lobe of the prostate was enlarged, bulging into the lumen The cut section showed it to be grayish with several small circumscribed nodules

Reddish mucosa covered with mucus was present in the gastro-intestinal tract The mucosa of the ileum, about 12 cm from the ileocecal valve, showed a small ulcer with elevated and rather soft and smooth margins The base of the ulcer was covered with reddish material. The peritoneal surface above the ulcer was smooth. Several small ulcerations in the rectum were combined with hemorrhagic zones There were a few small-sized polyps throughout the large intestines

The pancreas was normal.

The mediastinum and bronchial nodes were, if any, only slightly enlarged, soft, and reddish.

Microscopic examination of the lungs showed some alveoli filled with a serum precipitate, others with a varying amount of polymorphonuclears, lymphocytes, and a few endothelial cells A few fields showed dark-stained, somewhat granular material suggestive of masses of bacteria

Microscopic examination of the liver showed the central vein to be distended, sinuses dilated and filled with erythrocytes There were some liver-cells in the region of the central zones,

these were either atrophic or fibrotic The liver-cells in other portions showed marked granularity of the cytoplasm

Microscopic examination of the spleen showed no marked difference between the pulp and follicles The pulp showed an increase in connective tissue, very many lymphocytes, and large endothelial cells Several of the cells showed light-stained myelocytes The sinuses were filled with erythrocytes

The sinuses of the lymph-nodes were dilated, as seen by microscopic examination, and contained large numbers of light-stained epithelial cells

In the tonsils there was a large area of necrosis which showed only the outlines of the cellular elements This portion was surrounded by many polymorphonuclears, lymphocytes, and endothelial cells

The small intestines showed a large area which was very well circumscribed and consisted of new formation of connective tissue and muscle fibers with very many nuclei present here Some of the fields showed very many blood-vessels lined by normal endothelial lining cells Sections of the mucosa of the small intestine showed an interruption of continuity These fields were surrounded by lymphocytes, endothelial cells, and few polymorphonuclears

The bones were of normal architecture and the spongiosa was thin In the bone-marrow were large numbers of small and large round cells with densely stained nuclei and only a small amount of cytoplasm Several enucleated erythrocytes and very few granulated cells were present, most of them being large and apparently corresponding to myelocytes The absolute number of these cells is apparently very small

CLINIC OF DRS JACOB MEYER AND MORRIS PARKER

MICHAEL REESE HOSPITAL

SUBARACHNOID HEMORRHAGE IN A CASE OF PURPURA HEMORRHAGICA

THIS case is of unusual interest because of the development of subarachnoidal hemorrhage in a case of purpura hemorrhagica

A. R. a female aged forty-eight years, was admitted on July 14 1929 complaining of pain in the right knee and numerous black and blue spots on the body The patient was well up until one year ago at which time she complained of severe pain in the knee. She was advised by a neighborhood physician to take a course of mud baths. Shortly thereafter she noticed the black and blue spots like severe bruises over her body A few days before admission to the hospital she had consulted her dentist because of severe oozing of blood from her gums. He advised her to consult a physician Her previous history is not of interest.

Physical examination revealed that the patient was a small nervous woman rather pale. Blood was oozing from the gums and the tongue was covered with blood There were numerous hemorrhagic areas, varying in size from a pin head to a half dollar distributed over the upper and lower extremities chest, and abdomen Fresh petechial hemorrhages and large ecchymoses were prominent in the skin The physical findings were otherwise negative. The spleen was not palpable. The blood picture on admission showed the following Hemoglobin 80 per cent erythrocytes 4 200 000 leukocytes 9900 polymorphonuclears 59 small monocytes 34 transitionals 6, basophils 1 coagulation time six minutes bleeding time nine minutes clot was soft and *non*-retractile platelets 12 000 to 15 000 fragility test normal, blood calcium 12 Wassermann and Kahn tests negative

The clinical impression was that the patient had a purpura hemorrhagica Such conditions as aleukemic leukemia, aplastic anemia, and sepsis were excluded Transfusion of whole blood was advised and 250 c.c. were given There was moderate clinical improvement manifesting itself by cessation of oozing

of blood The effects, however, were temporary A week later another blood transfusion was given A severe reaction occurred For a week the hemorrhage from the gums, mouth, and the subcutaneous tissue continued On July 31, 1929, 5 c c of the patient's blood was withdrawn and reinjected into the buttocks (intramuscularly) A severe reaction occurred The following day, August 1, 1929, the patient was restless, vomited, and had involuntary urination She became stuporous and her temperature rose to 101 8° F August 2, 1929 the stupor continued, fever persisted, vomiting was projectile, occipital headache, rigidity of neck, with pain on motion were present Kernig's and Brudzinski's signs were negative Ophthalmoscopic examination revealed pallor of the disks

August 3, 1929 a spinal puncture was performed and 15 c c of spinal fluid removed The spinal fluid was blood-tinged and under increased pressure When centrifuged the fluid was xanthochromic The impression at this time was meningo-encephalitis or repeated small hemorrhage in the subarachnoid space, due to purpura hemorrhagica

August 4th headache and rigidity diminished after puncture Blood-smear at this time showed 6 per cent myelocytes This suggested the possibility of leukemia, which we had considered early in diagnosis Magnesium sulphate, 50 per cent saturated solution, was administered per rectum

August 6th the patient was given 50 per cent magnesium sulphate, 6 ounces, per rectum, twice daily and appeared less drowsy Leukocytes, 14,000, polymorphonuclears, 71, myelocytes, 6 Drowsiness increased and oozing from mouth continued

August 7th patient restless and irrational The retinæ were pale, lemon-yellow The left arm was possibly weaker than the right, and the neck was rigid Intravenous glucose, 50 per cent, was given on this day and the day following

August 9th the patient was more alert and took fluids by mouth The temperature remained elevated and anemia had developed Leukocytes 13,200 and the platelets were increased and seemed large in size

August 10th temperature was 101° F Patient had become less stuporous, but was rather restless, however there were periods of euphoria She was unable to express herself intelligently, her words became jumbled, and her memory was poor There were periods in which she lapsed into a stupor Kernig's sign was positive, the neck was rigid Magnesium sulphate, 50 per cent., 6 ounces, given per rectum

August 13th a spinal puncture was done and the fluid was noted to be clear, xanthochromic, not under increased pressure, and contained globulin and microscopic red cells When the red cells were dissolved there were 55 leukocytes with 91 per cent. lymphocytes The Lange was 0,000,220,000

August 14th the patient had become stuporous over night and her muscles were flaccid There was no Kernig, no rigidity of the neck Her temperature rose to 103° F and she had involuntary urinations Leukocytes were 23,200, polymorphonuclears 83 per cent Cheyne Stokes breathing was present, 1000 c.c. of saline solution were given subcutaneously

August 16th patient was euphoric, had olfactory hallucinations, and complained of headache Temperature was normal Examination of the blood showed the hemoglobin 75, leukocytes 16,900, erythrocytes 3,610,000, platelets 43,000

August 18th the patient complained of severe headache, mispronounced words, and rambled Erythrocytes were 4,320,000, hemoglobin 75, leukocytes 18,100, and polymorphonuclears 54 per cent.

August 20th the patient's temperature began to rise last evening, 101° to 102° F She had a severe headache with severe bleeding from the gums Blood examination revealed the following hemoglobin, 75, erythrocytes, 4,690,000, leukocytes, 16,400, platelets, 28 per cent , polymorphonuclears, 60 per cent

August 22d the patient had normal temperature and no complaints. Hemoglobin was 70, leukocytes 14,300, polymorphonuclears 60, platelets were scarce

The course continued in this way, the temperature gradually decreasing The general condition of the patient began to improve from about this last date Oozing of blood from the

mouth would occur at times, but the subcutaneous tissue and muscles were free The patient made steady clinical improvement, although the blood-picture (platelets) did not change materially The patient was discharged one month later, September 22d, as improved The table on page 1209 gives the blood studies

BLOOD EXAMINATIONS

Dat	HB	R. B C.	W. B. C.	Differential count.						Platelets.	Mon.	Mye	C ll coa t
				N	SM	LM	T	E	B				
7/15	80	4 240 000	9 900	59	33		6		1	12–15 000			100
/16	80	4 ,00 000	7 000	48	42	5	1	2		45 000	2		100
7/18	85	5 100 000	5 800	62	25	8	1			35–45 000	4		100
7/19	85	4 750 000	6 600	50	38	8	1			15 000	3		100
7/20	85	4 900 000	6 000	56	38	5	1			15 000			
7/24	95	4,300 000	7 000	60	13	17	7			As before	3		100
7/26	90	4,850 000	10 400	63	14	14	8		1	Unchanged			100
8/ 1	85	4 800 000	7 000	74	11	10	2			As before	3		100
8/ 3			7 400	57	16	18	1			Rare[1]	2	6	
8/ 4	80	4 000 000	14 000	71	1	9	13			Unchanged		6	
8/ 6			13 600	63	13	14	2				7	1	
8/ 9	75	3 500 000	13 200	64	22	9	4			60–100 000	1		
8/10			15 900	55	19	16	7			40–50 000	3		
8/12			16 000	67	22	10				40 000	1		
8/14	70	3 650 000	23 200	83	1	5	5	2		100 000			
8/17	75	3 710 000	16 900	76	21					43 000	2		
8/18	75	4 320 000	18 100	54	40					51 000	3		
8/20	70–75		16 400	60	36					28 000	4		
8/22	70		14,300	69	29					None seen	2		
8/23										16 900			
8/26	80–85	3 960 000								23 000			
8/27	70		12 300	70	30					Occas. large			
8/29	70		10 000	72	24					Very scarce			
8/31	70		9 200	71	29					15 000 large.			100
9/ 2	75	4 050 000	6 800							28 000			
9/ 4	75	3 980 000	11 600	55	45					24 000			100
9/ 7	75	3 760 000	6 750	64	36					37 000			
9/11	80	4 530 000	5 500	53	47					26 000			100
9/16	80	4 260 000	9 600	70	30					Few			
9/20	70	4 800 000	6 500	56	40		4			22 000			

Repeated blood-cultures—negative. Fragility tests—normal.

CLINIC OF DR JOSEPH K CALVIN

Cook County and Michael Reese Hospitals

UREMIA IN CHILDREN

I wish to present to you today 2 cases of uremia in children, which represent, however, two distinct types of the condition

Case I Acute Convulsive Uremia.—This patient is a boy aged eight years. He was well until eight days before admission to the hospital three months ago At the onset he developed a rather severe attack of *tonsillitis* Seven days after the onset of the tonsillitis, when he was feeling well again and the temperature had been normal for several days there was a sudden onset of another group of symptoms. He complained of *headache* which rapidly increased in severity *marked dimness of vision* and *vomiting* Within a few hours he developed generalized *convulsions* between which he was *comatose*. The convulsions were epileptiform in that they lasted a few minutes and consisted of a tonic clonic, and comatose stage In this condition he was admitted to the hospital

Examination on admission to the hospital revealed the following important findings The patient was *comatose* with generalized *convulsions* recurring about every half hour and lasting several minutes. The deep reflexes were increased transient paresis of the extremities was present and transient Babinski reflexes were present at times. A generalized moderate degree of *edema* was present, involving the face as well as all the subcutaneous tissues extremities etc. The temperature ranged between 100 and 103 F The *blood-pressure was 170 systolic* and 110 diastolic. The *urine* (catheterized specimen) showed a high specific gravity of 1 040 was dark red (smoky) in appearance containing a one plus albumen many *red blood-cells* a moderate number of white blood-cells a few granular casts, and no sugar The eye grounds were negative. The *blood chemistry* revealed a urea nitrogen of 25 mg per 100 c.c. of blood (normal value 10 to 20 mg) and a non protein nitrogen of 53 to 60 mg (normal 25 to 40 mg) the chlorides were 534 mg (normal 450 to 500) the CO_2 46 c.c. per 100 c.c. of plasma (normal 50 to 75) the water content 81.52 per cent., the cholesterol 193 mg to 200 mg per 100 c.c. of blood (normal 125 to 200) the serum albumen was 6 85 per cent (normal 4 6 to 6 7 per cent) and the serum globulin 1 21 per cent (normal 1 2 to 2.3 per cent.) the sugar 136 mg The Wassermann on the spinal fluid and blood was negative. The blood-count was 26 000 leukocytes which rapidly fell to 15 000 on administration of fluids—the differential count polymorphonuclears 80 per cent., lymphocytes 20 per cent.

Course and Treatment—The treatment of this uremic attack consisted of (1) lumbar puncture, (2) posture, (3) venesection, (4) intravenous solutions, (5) forcing fluids, (6) sedatives, and (7) heat

Spinal Puncture—A spinal puncture was immediately performed to relieve intracranial pressure The fluid was under markedly increased pressure, clear, negative globulin tests, cell count 5 per cmm , 40 c c were removed

Posture—The patient was propped up in bed with the head well elevated in an attempt to reduce the possible cerebral edema The head of the bed was elevated

Venesection was performed with the withdrawal of 200 c c of blood (300 to 500 c c may be withdrawn in older children or adults)

Intravenous Solutions—One hundred and fifty c c of *20 per cent glucose* was then given *slowly* intravenously The blood-pressure dropped from 170 systolic and 110 diastolic to 145 systolic and 90 diastolic during this procedure The convulsions and coma subsided for six hours and then recommenced Fifty c c of *2 per cent magnesium sulphate solution* was then given intravenously, very slowly over a period of one-half hour (As much as 150 c c may be given) This is extremely valuable therapy [1] Blackfan uses a 1 per cent solution of magnesium sulphate intravenously and injects about 15 c c per kilogram of body weight at the rate of 2 c c per minute A fall in blood-pressure is the best index as to the total amount necessary The blood-pressure readings are taken on the other arm while the solution is being injected When the systolic pressure falls to 120 the injection may be discontinued The effect lasts five to twelve hours and the injection may be repeated every twelve to twenty-four hours, for several days if necessary The magnesium sulphate given in this manner acts as a diuretic, but not as a cathartic, has a definite sedative action, relieves the cerebral edema by altering the osmotic relations in the body fluids and thus relieves the cerebral pressure symptoms of vomiting, headache, coma, delirium, convulsions, and reduces the blood-pressure The blood-pressure fell from 150 to 110 mm of mercury during

this procedure and the convulsions subsided permanently, although muscular twitchings and occasional delirium remained. Large amounts of calcium have been administered intravenously in some cases, with reported favorable results, but the author has had no experience with this method. A caution is to be observed in the intravenous administration of solutions in this condition. Because of the high blood pressure which is usually acute, rapidly rising, and recent, the heart does not have an opportunity to accommodate itself to the hypertension and is under considerable strain, and so, if a volume of fluid is introduced *rapidly* into the blood stream, the blood pressure may rise considerably for a few minutes which may cause an acute dilatation of the heart.

Forcing Fluids.—Whether it is advisable or inadvisable to restrict fluids in nephritic edema is a much debated question, but when acute convulsive uremia is impending or established no doubt remains. *Fluids should be pushed* by every avenue possible. In this patient the stomach was washed out with a weak bicarbonate of soda solution and after the vomiting and convulsions ceased, but before he would take fluids voluntarily, he was given 50 per cent. glucose solution and sweetened orange juice by nasal catheter, about 3 ounces each (6 ounces total) every three hours. Retention enemas of 4 ounces of 5 per cent. glucose were also given every three hours. No fluid, of course, was given subcutaneously, as the patient was already edematous in these tissues. If he were not, however, 5 per cent. glucose would have been administered subcutaneously (hypodermoclysis). *Saline solutions should not be administered* by any avenue, as there is evidence to show that sodium chlorid retained in the tissues in nephritis increases the edema and precipitates or increases the uremic syndrome.

Sedatives.—*Morphin* is the most important and satisfactory for the purpose, $\frac{1}{8}$ grain was given every six hours until the convulsions were controlled. This was dissolved in 2 c.c. of a *25 per cent. magnesium sulphate solution* and given intramuscularly because the synergistic action of the two drugs greatly enhances the antispasmodic value without adding to the danger

of narcosis Chloral and bromids may be given rectally, although none were used in this case Phenobarbital may be used Ether may be administered as a last resort to control the convulsions

Magnesium Sulphate—From 1 to 3 ounces of a saturated solution was given by stomach-tube daily as soon as the vomiting stopped Of course, after the patient would take this voluntarily by mouth, the use of the stomach-tube was discontinued Magnesium sulphate was continued until the systolic blood pressure was under 110 In the presence of edema, magnesium sulphate given in these doses may not cause catharsis

Heat—Continuous moist or dry heat (hot-water bags) applied to the lumbar region is advisable to relax the spasm, if possible, of the kidney arterioles and thus promote increased secretion of urine

Dry heat sweats by means of an electrically lighted cradle placed over the entire trunk and extremities and applied cautiously for one-half to one hour twice daily, may eliminate a liter or more of water during the stage when the kidneys are unable to do so This sweating lowers the blood-urea considerably and helps to eliminate other toxic products in the sweat As soon as the output of urine increases to 20 ounces or more daily (which usually happens within a few days) the sweats should be discontinued Children become very restless while under the dry heat apparatus and the pulse-rate increases considerably Consequently this phase of the treatment must be carefully supervised to prevent too much exhaustion and depression of the patient

Within thirty-six hours after beginning the above therapy the convulsions had permanently ceased, the temperature was normal, the child was bright and rational, and the blood-pressure was 110 systolic Within a few more days the blood-pressure was 104 systolic and 76 diastolic

Now that the child had recovered from the acute convulsive uremia, the remainder of the *treatment* was directed toward the underlying *acute hemorrhagic (glomerular) nephritis*

Rest in Bed—*Absolute confinement to bed* is essential until the edema has disappeared, the blood-pressure is normal, and

the urine is normal, or at least until only a trace of albumen and an occasional microscopic red cell is present. Allowing the patient up too soon is one of the commonest mistakes The average time in bed is at least a month If, after being up and around, the patient's urine again shows abnormal findings, he must be returned to bed until it clears up

Warmth is necessary It is known that cold, exposure to wet, etc., is often the cause of the onset of an acute nephritis Exposure to chilling certainly will cause a relapse I always advise that the patient wear woolen underwear even while bedridden and that the bed be away from the window

Diet.—*Low Protein and Low Salt*.—Regarding *diet* we must attempt to rest the kidney and so prescribe a diet which will require least work for the kidney As *protein and salts are eliminated with difficulty* the diet should be poor in these substances and yet have sufficient caloric value to maintain weight The objection to allowing *milk* to make up the major portion of such a diet is that milk contains considerable protein (35 to 40 gm. per liter—quart), and is also high in salt content If enough milk is taken to fulfil the entire caloric requirements the protein and salt allowance will be overstepped One gram to one and a half grams of protein per kilogram per twenty-four hours is sufficient to maintain nitrogen equilibrium (so that tissue proteins are spared) The amount of milk necessary to provide this amount of protein (minimum protein requirement) may be given provided it does not exceed a quart, as milk protein is a complete protein and readily digested The elimination of excess salt by using unsalted butter and salt-free bread and not adding salt to the cooking or table food is sufficient restriction

Other Foods to Make up the Caloric and Vitamin Requirements.—Other foods are then added to the diet, as fruits and plenty of fruit juices containing liberal amounts of sugar, unsalted butter, cream, creamed soups without meat stock, ice cream, rice, well-cooked cereals, potato, salt free bread, vegetable oils, simple puddings without egg, as cornstarch, rice, etc. Ripe bananas are excellent food in acute nephritis They are easily digested, rich in vitamins B and C, high in carbohydrate, and

low in protein Later, cooked vegetables are added except beans and peas, because of their high protein content Banana, cream, butter, and sugar are excellent foods for increasing the calories in the diet and making up the caloric requirements After one month, if the urine is practically negative, egg yolk, a rich source of iron, calcium, fat, and vitamins A and D are added to the diet Later, and cautiously, egg white and meats are added

"*Sugar*" *Days*—During the acute stage while considerable hematuria is present a "sugar day" is observed twice a week, the patient receives only well-sweetened and diluted fruit juices, ad lib , 1 to 2 quarts On these days the blood will often temporarily disappear from the urine

Spices, etc—Meat extractives, such as soups and meat juices, condiments and spices, as well as coffee and tea are absolutely forbidden

Fluids—If no edema is present fluids should be forced If edema is present there is considerable debate as to whether fluids should be forced At one extreme is Volhard,[2] who believes that during acute nephritis there is a vasomotor spasm of the vas afferens leading to the glomerulus He, therefore, believes in restricting all liquids and foods for a period of three to five days at the onset, the patient only receiving fruits and fruit juices in moderate quantities This, according to Volhard, causes the blood-pressure to fall, the edema to diminish, and the urinary output to increase Then the fluids are gradually increased An excess of fluid early, according to this theory, tends to throw excessive work on an already injured kidney and may increase the blood-pressure to the point of cardiac failure At the other extreme are those[3] who advocate forcing fluids in every case so that toxins may be diluted and diuresis established Some believe that the edema acts as a protective mechanism to dilute the toxins

I believe that the amount of the fluid intake of every edematous case of acute hemorrhagic nephritis, not in a state of impending or actual uremia, should be judged on its own merits Beginning with 800 to 1000 c c in twenty-four hours, if gradually

increasing this fluid intake increases the edema or the blood-pressure, the fluid intake should then be reduced to the point where it does not increase the edema or the blood pressure Otherwise, the fluid can be gradually increased to a liberal intake unless indications of increasing edema or blood-pressure appear Increasing edema can be detected only superficially by inspection Better ways are (1) Daily weighings, any marked increase or decrease in weight indicates a change in the amount of edema, (2) measuring the output of urine The output of urine should, of course, be almost as great, if not greater, than the intake of fluid, unless much water is lost by the application of hot air baths (dry heat) or diarrhea Any marked discrepancy between the intake and output indicates an increase or decrease of the edema (3) The time of disappearance of the wheal of .2 c.c. of saline injected intradermally (Aldrich and McClure test[4]) When no edema is present the wheal should require at least sixty minutes to disappear, while the greater the edema, the shorter the time necessary for its disappearance

Drugs have a limited application in the treatment of uncomplicated acute glomerular nephritis Laxatives and magnesium sulphate have been mentioned They should insure the proper daily evacuation Diuretics, such as the purine group, and ammonium chlorid, salyrgan, etc , are absolutely contraindicated, as they tend to increase the hematuria and nitrogen retention Bland forms of iron, as liquor ferri et ammonii acetatis, to combat the anemia may be given Digitalis may be necessary if signs of cardiac collapse appear

Daily tepid or warm baths are valuable

Blood —Intramuscular injections of 30 to 60 c c. of whole blood from the child's mother or father were given in our case every third day for three doses This procedure, which is easy to perform, I believe is of great value for the following reasons (1) Adult blood often acts similar to an antitoxin when injected into children, inasmuch as the adult is usually relatively immune to the throat, nose, and gland infections so common in children, especially if the adult had these infections as a child, i e injection of adult blood is known to protect against measles

As most cases of acute hemorrhagic nephritis in children either accompany or follow shortly an acute throat, nose, ear, or gland infection, I believe the injection of adult blood intramuscularly into the child is of value in controlling the accompanying infection and toxemia, and thereby controlling the focus of the trouble as early as possible

2 A considerable anemia usually accompanies the nephritis, partly due to the toxemia and partly from the hematuria Intramuscular blood, as does intravenous, stimulates the hematopoietic organs and aids to overcome the anemia, besides, the hemoglobin and its products are absorbed from the site of the injected blood and furnish available materials for blood regeneration

3 Injected blood acting as a foreign protein stimulates the entire reticulo-endothelial system, which has much to do with the defenses of the body against infections or toxic agents [5]

4 The procedure may diminish the hematuria immediately Its value in this respect is still under investigation to determine whether bleeding from the glomeruli can be thus influenced

Case II True Chronic Uremia—A W, a white boy, nine years of age, was brought to the hospital three months ago because of the following complaints Weakness and pallor for the past four years The child was first noticed to be pale about four years ago and was treated for anemia The tonsils were removed at that time There had been no recent acute illness or febrile disturbance Two years later heart trouble was diagnosed because of pallor, weakness, and slight dyspnea. The child remained in bed for five weeks at this time

No cough, headache, vomiting, or edema had been present The only urinary disturbance was nocturia and occasional enuresis

The birth and developmental history were negative

The father and mother and an older child, eleven years, were in excellent health No deaths in the immediate family

Past Illness—Measles, pertussis, and influenza when two years of age, no complications, complete recovery

Examination at the time of admission to the hospital revealed a well nourished, normal height, very pale child, not acutely ill Positive findings were one carious tooth, a small fragment of left tonsil present, the heart was not enlarged, but a slight systolic bruit was present at the apex, otherwise the results of the physical examination were negative The eye-grounds were normal on retinoscopic examination

The blood-pressure on several examinations varied from 100 to 106 systolic and 65 to 70 diastolic

The urine showed a trace to one plus of albumen but was microscopically negative on repeated examinations.

The blood chemistry showed a urea value ranging from 94 to 123 mg., creatinin of 8 mg. per 100 c.c. The cholesterol was 150 mg.

The hemoglobin was 50 per cent. the erythrocytes 2 550 000 the leukocytes 5200 polymorphonuclears 68 per cent., lymphocytes 10 per cent. and monocytes 22 per cent.

The von Pirquet test was negative. The Wassermann test was negative.

The kidney function tests revealed the following. The phenolsulphonephthalein output was 10 per cent. in three hours (normal about 70 per cent.). The specific gravity was fixed at a very low level in the concentration and dilution tests, varying from 1 002 to 1 005 throughout the twenty four hours.

The intradermal absorption time of normal saline was normal—more than sixty minutes.

Course.—The weakness, asthenia, increased the patient becoming bedridden. Gastro-intestinal symptoms, as nausea and vomiting, loss of appetite, persistent hiccough, great thirst, diarrhea and stomatitis, slowly developed and insidiously became worse. The respiration became at first irregular, later developed the Kussmaul air hunger type, slow and deep, characteristic of acidosis. The breath had a uriniferous odor. Persistent and severe headache developed. Lethargy followed by drowsiness appeared which gradually passed into stupor and coma. Before the stage of coma was reached restlessness and at times delirium alternated with the lethargy. The muscles of the extremities twitched, the reflexes were increased but no abnormal reflexes, as the Babinski, were present. Convulsions did not occur. There were transient attacks of amaurosis. During the development of the above symptoms there was rapid loss of weight although no edema had been present, and a subnormal temperature.

The *blood pressure* in this patient did not increase although most commonly in chronic uremia the hypertension is marked but later falls gradually until death ensues. The *urea nitrogen* gradually increased to 170 mg. per 100 c.c. of blood, the non-protein nitrogen to 250 mg., the creatinin to 12 mg., the CO_2 content of the blood fell as low as twenty volumes per cent.—above forty-five is normal—indicating a severe acidosis. The *urine* remained of a low and fixed specific gravity and contained a one plus albumen and occasional hyaline casts. The leukocytes of the blood were increased from 11 000 to 23,000 with an increase in polymorphonuclear leukocytes from 75 to 90 per cent. The red blood-cell count dropped to 2 000 000 with 40 per cent. hemoglobin, indicating a severe anemia.

Treatment.—*True chronic non-convulsive acidotic uremia* is not amenable to any form of treatment and is invariably fatal. It is the terminal stage of insidious chronic progressive glomerular or interstitial nephritis, resulting in a permanent absolute renal insufficiency. The progress may be checked at times for short durations.

The individual manifestations can be treated By carefully cleansing the mouth the saliva, heavily laden with urea, is less likely to produce stomatitis and secondary parotitis The nausea and vomiting may be relieved by washing out the stomach with dilute sodium bicarbonate solutions and the administration of atropin For the nervous and motor symptoms, restlessness, delirium, and twitchings, morphin with magnesium sulphate intramuscularly or chloral hydrate per rectum, are of value Unless diarrhea or vomiting is present, 1 ounce of a saturated solution of magnesium sulphate is given daily by mouth Warm baths daily prevent itching and irritation of the skin from the urea excreted in the sweat Hot-air baths have recently been employed by Allen[6] with benefit, provided there is no severe cardiac or asthenic contraindications By means of dry heat as much as 4 liters of water may be eliminated as perspiration through the skin without prostration and the urea often reduced from 150 to 60 mg , at least temporarily As urea retention is generally held responsible for the symptoms of chronic uremia, naturally any factor causing a fall of blood-urea content ameliorates the symptoms Venesection should only be used for excessively high blood-pressure, which is not usually much of a factor in the chronic nephritis of children

Tests for Chronic Uremia—As *indican* is one of the easiest substances for the kidneys to eliminate, its retention in the blood is always an indication of a poorly functioning kidney—so poorly functioning that true chronic uremia is imminent or present A simple test for indican in the blood, and so a test for chronic uremia, is as follows

The test is known as Rosenberg's modification of Jolle's indican test

1 To 5 c c of serum add 5 c c of distilled water

2 To this add 10 c c of 20 per cent trichloracetic acid, and filter

3 To the filtrate add 5 minims of a solution of 5 per cent thymol in 95 per cent alcohol

4 Then to the filtrate add an equal volume of 0 5 per cent ferric chlorid solution in concentrated hydrochloric acid

5 Allow this to stand for two hours Then shake with 3 c.c of chloroform When indican is present the color changes from red to violet

Ehrlich's *diazo reaction* can be obtained in the blood in impending or established chronic uremia.[7] This is another good test

Theories Regarding the Etiology of Uremia—The theories as to the cause of these two types of uremia are many and varied

Acute convulsive uremia is not dependent on renal insufficiency or retained nitrogenous products We have seen in Case I that this form of uremia can occur with a blood urea only slightly increased above normal. Hypothetical unknown poisonous substances have so far not been proved, nor would their assured presence explain why they act at one time and not at another Volhard[8] believes that this form of uremia is due to cerebral edema, the so-called "wet brain," an intra and extra-cellular edema of the brain causing it to become compressed in the closed cranium The compression of the smaller vessels of the brain and the resulting anemia of the cortical center is followed by convulsions If the edema is intracellular there will be no change in the pressure of the spinal fluid All the symptoms can be produced by cerebral compression How is the cerebral edema produced? Convulsive uremia occurs most frequently during acute glomerular nephritis, which is not accompanied by nearly as much edema as nephrosis, in which condition it does not occur Volhard again explains that in acute glomerular nephritis there is generalized arterial contraction with rapidly increasing blood pressure, which causes an increased blood flow to the brain with increased transudation of fluid into the brain substance

Blackfan relieved the symptoms of vomiting, headache, visual disturbances, coma, delirium, and convulsions with intravenous injections of 1 per cent magnesium sulphate solution and by large doses of magnesium sulphate by mouth. The blood-pressure returned to normal and the edema largely disappeared after this treatment also The hematuria, non protein nitrogen, and oliguria were not influenced by the magnesium sulphate

Furthermore, in several autopsies on patients dying during acute convulsive uremia, marked edema of the brain was found The spinal fluid may not appear to be under increased pressure because the foramina of the brain may be compressed and closed by the edema Consequently he believes that the symptoms of acute convulsive uremia are due to edema of the brain with resulting increased intracranial pressure The blood-pressure then rises secondarily as a result of the increased intracranial pressure as a compensatory mechanism to prevent bulbar anemia (Cushing)

Marriott believes that the hypertension in acute glomerular nephritis is due to a general capillary constriction throughout the body, and holds that the uremic symptoms are due to the same toxin causing the capillary damage

The general conception of *true chronic uremia* is that of an intoxication produced by retained products of renal excretion The urea forms the bulk of the retained products It has been demonstrated experimentally[9, 10, 11] that very markedly increased urea retention in the blood of man and experimental animals will reproduce the symptoms of chronic uremia Elwyn[12] has briefly reviewed the literature in favor of the theory that very marked urea retention can cause chronic uremia He leans toward this theory Allen,[13] by means of dry heat, stimulating the vicarious function of the skin for the kidneys, reduced the blood-urea from 180 to 60 mg in cases of chronic nephritis The symptoms of chronic uremia were correspondingly relieved, confirming the conception that chronic uremia is due to retention Superimposed on this type of uremia is a condition of *acidosis*, due to a diminution in the alkali reserve in the blood, resulting from an attempt to neutralize the sodium phosphate which is retained in the blood with the other products of excretion The symptoms referable to the acidosis are especially the slow and deep breathing

Andrews[14] experimentally reproduced uremia in dogs by a different method He does not attempt, however, to distinguish acute convulsive uremia from chronic true uremia, but attempts to explain uremia in general, a decided confusion in his work,

inasmuch as clinically the two types appear so distinctly The symptoms and signs of his experimental uremia in dogs resembles the acute convulsive uremia of humans His nephrectomized dogs lived as long as ten days and developed a very high blood urea retention without showing signs of uremia Consequently, he states that the retention of waste nitrogen is not the cause of toxemia in uremia He produced the uremic and edemic syndromes in dogs by injecting hypertonic chlorid solutions into animals that were unable to eliminate them because of a suppression of urine from a pre-existing acidosis or double nephrectomy The chlorids and water, according to Andrews, make their way from the blood to the tissues, especially to the organs which hold most chlorid—the liver and the brain This causes increased permeability of the liver cells, disintegration of the cells, liberation and loss of calcium, and toxic protein disintegration products from the cells, and so disintegrating liver cells are the source of the uremic toxins Welker[15] goes still further, and has identified by the precipitin reaction this disintegrating liver protein in the blood and urine It acts as a foreign protein, causes increased permeability of the kidney, and is excreted in the urine loosely combined with the blood proteins which combine with and detoxicate this foreign protein The convulsions in the dogs could be controlled and recovery brought about by massive doses of calcium given intravenously

In short, Andrews reproduced the uremic syndrome by disturbing the acid base equilibrium, causing an acidosis, and then the mineral-salt balance Inasmuch as he showed that water and salts can be fixed in the tissues with suppression of urine and uremia without abnormal histologic changes in the kidney, he believes that uremic changes are extrarenal in origin His theory explains very well acute convulsive uremia in the human when, as in Case I, there is not much increase in the blood urea and a marked increase in blood pressure and edema

Prognosis —Because of the vast difference in prognosis in these two types of uremia it is highly essential that acute convulsive uremia be differentiated from true chronic uremia The acute hemorrhagic types of nephritis are by far the most

common forms in children, acute convulsive uremia occurs most frequently in the hemorrhagic types of nephritis, consequently, acute convulsive uremia occurs much more frequently in children than does chronic uremia, which is a terminal stage of chronic nephritis—a relatively infrequent condition in children

The only influence acute convulsive uremia has on the prognosis of the underlying nephritis is the immediate danger of death if the uremia is not rapidly and adequately treated Uremia is the chief cause of death in acute hemorrhagic nephritis After the acute uremia has subsided the nephritis may entirely disappear within a few weeks, as in Case I, especially as the underlying nephritis is usually the acute glomerular (hemorrhagic type), following an acute streptococcal infection, from which 90 per cent of cases completely recover The most common mistake made in the diagnosis in these conditions is the assumption that because uremia has supervened that a chronic progressive nephritis is present The acute convulsive uremia may, in fact, usher in the acute nephritis, as in Case I It is highly essential then to carry the child through the acute uremic manifestations, as uremia only affects the immediate prognosis and has no effect on the chronicity, the patient showing no greater tendency to acquire chronic nephritis [16]

If, during the course of nephritis in childhood, symptoms of impending or threatened acute convulsive uremia appear, they should be vigorously treated Such symptoms are a rapidly increasing blood-pressure over 130 systolic, vomiting, epigastric pain, headache, visual disturbances, and restlessness The steadily rising blood-pressure presaging the onset of uremia is the most reliable sign The treatment then is to force fluids by every avenue available, give 1 to 3 ounces of a saturated solution of magnesium sulphate daily by mouth until the blood-pressure falls below 120, perform a spinal puncture to relieve intracranial pressure, elevate the head of the bed, give warm baths, and administer sedatives, if necessary

The treatment of the actual attacks has been described under Case I

The essential differential points between the two types are

Acute Convulsive Uremia	*True Chronic Uremia*
1 History of recent acute infection, especially scarlet fever tonsillitis, otitis media	No history of recent acute infection History of chronic nephritis
2. Presence of acute hemorrhagic nephritis most commonly	Presence of chronic progressive nephritis
3 Acute onset	Insidious onset
4. Convulsions	Usually no convulsions.
5 Rapidly increasing hypertension	May or may not be hypertension
6. Edema usually present	Edema often absent.
7 Air hunger not pronounced	Air hunger Kussmaul breathing marked
8. Urine usually shows small quantity suppression or anuria high specific gravity albumen blood and granular casts.	Urine shows often large quantity low and fixed specific gravity small amount of albumen and hyaline casts may however show the urinary picture of chronic glomerular hemorrhagic, nephritis
9 Blood chemistry Urea and non protein nitrogen slightly to moderately elevated creatin in usually normal CO_2 combining power usually moderately lowered.	Blood chemistry Urea and non protein nitrogen very markedly elevated CO_2 combining power markedly lowered creatinin markedly elevated usually over 5 mg per 100 c c. of blood.
10. Permanent response to proper therapy	Temporary if any response to therapy
11 Coma is a frequent condition in both types.	

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CLINIC OF DR I PILOT

Lutheran Deaconess Hospital

PUTRID EMPYEMA AS A POSTOPERATIVE COMPLICATION

In previous observations of the postanesthetic pulmonary infections several cases of putrid empyema were studied and in all there was noted the development of a well-defined pulmonary abscess or gangrenous process with marked clinical symptoms before the complicating empyema appeared.[1] We have always emphasized the bacteriology of such lesions to determine the source and pathogenesis of the infection. When the fusiform bacilli and its symbiotic spirochetes appear in an abscess or in pus of the pleural cavity, it is reasonable to believe that these organisms come from the mouth where they are present in abundance. The most natural route in cases with general anesthesia would also be by inspiration of the oral secretions. In our experiments we have found that by adding lipiodol to teeth scrapings and tonsillar débris and injecting the mixture intratracheally into rabbits, suppurating and gangrenous lesions result in the lung and pleura. One striking feature in the experiments was the development in the rabbit of an empyema of a putrid character without a broken-down abscess or gangrenous cavity of the lung.

In the following case is illustrated a clinical instance of the development of a putrid empyema without well-defined clinical manifestations of an abscess or gangrene of the lung.

[1] N., Male white thirty-five entered on September 16, 1929 with complaint of a severe acute pain in the epigastrium of eighteen hours' duration. The patient was apparently well until he developed a sudden excruciating

[1] Pilot and Davis: Pulmonary Abscess, Gangrene and Bronchitis: Arch. Int. Med., September 1924, 34: 313–354.

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pain in the upper abdomen The pain continued without relief He seldom had epigastric distress and mentioned that he had burning pain in the epigastrium during the previous winter On examination, the patient appeared desperately ill The abdomen was slightly distended, very tense, and tender Leukocyte count at this time was 19,200, urine showed slight trace of albumin A diagnosis of perforated duodenal ulcer was made and under ethylene and ether anesthesia the abdomen was explored The first and anterior portion of the duodenum revealed a larger perforation 1 cm in diameter

Fig 182 —Putrid empyema following general anesthesia At no time was a pulmonary abscess demonstrated

The ulcer was excised and closure made transversely The patient was under the anesthetic for fifty-five minutes During the following five days, September 16th to 21st, his temperature varied from 99° to 100 8° F from the 21st to the 26th 100° to 101° F , on the 26th he complained of severe pain in chest Marked coughing but no expectoration was noted on the 27th, when his temperature rose to 102° F On the 28th the pain was absent and physical examination suggested evidences of fluid The abdomen was always soft and

the wound healed By paracentesis a clear serous fluid was withdrawn which contained polynuclears in few numbers but no bacteria From the 28th of September to October 5th the temperature remained below 102° F from October 5th to 23d the fever varied from 102° to 104 F On the 18th slight expectoration of sputum with no odor occurred and in sputum examinations fusiform bacilli spirochetes and cocci were reported The white blood-count on the 19th was 33 800 Signs of fluid in chest were now obvious and on paracentesis a very putrid greenish pus was obtained (Fig 182) On the 23d a resection of ribs was performed Although the temperature seldom exceeds 101 F the patient continues to be quite ill and at the present time he appears very septic and the outlook unfavorable

Of great interest was the bacteriologic examination of the pus In smears enormous numbers of bacteria were present, chiefly Gram positive cocci, and fusiform bacilli in short and long thread like forms A scant growth was obtained on blood-agar of very fine colonies of indifferent streptococci, and in the anaërobic cultures the same streptococcus was observed in larger colonies No other organisms appeared in either cultures In the differential diagnosis we were concerned with an infection coming from below, in the form of a subdiaphragmatic abscess, with extension through the diaphragm or a primary infection from the respiratory tract In the first paracentesis I had failed to mention that Dr Henderson, the surgeon, had made one exploratory puncture low, and he stated that he did not obtain any pus from the region of the diaphragm However, as this would not exclude an infection from below the diaphragm, for differentiation we laid great stress on the bacteriology If the foul pus originated from the abdominal cavity the cultures would have shown large numbers of colon bacilli Instead the organisms were like those observed in the oral cavity and these would more likely gain entrance through the respiratory tract

To explain our case it is necessary to assume that an aspiration bronchopneumonic process developed following the operation Usually with liquefaction necrosis by the anaërobic bacteria and with the formation of a pulmonary abscess the patient expectorates typical foul suptum on the twelfth to fifteen day This was prevented by the rapid extension to the pleura and the quick formation of fluid which collapsed the lung

At the present time (January 17, 1930) the patient appears to be greatly improved The temperature is normal, drainage through thoracic wound slight and no longer putrid Such recovery is unusual, for the mortality in putrid empyema has been very high in our experience

LUTHERAN DEACONESS HOSPITAL

PAROXYSMAL HEMOGLOBINURIA

Paroxysmal Hemoglobinuria —Report of a case due to cold and syphilis

A white male patient aged forty nine first consulted me (Dr F) two years ago complaining of an acute attack of severe pain in the right hypochondrium associated with a severe chill dyspnea and a sensation of a lump pressing against the heart.' The pain radiated to the right scapula and was so intense the patient was compelled to remain fixed in one position A cup of hot coffee promoted a sense of body warmth and seemed to give considerable relief About one half hour after the onset of the pain he felt a strong desire to void urine which when passed, was of a reddish brown color He was told that during the attack his face assumed a peculiar gray white hue while his lips were a deep purple The pain persisted more or less during the following three hours and the urine gradually returned to normal on the following day This attack was followed by another three days later coming on while the patient was exposed on a cold day as was the case with the first attack.

Inquiry regarding other gastro-intestinal cardiac respiratory urinary and nervous symptoms was entirely negative. He had always been a robust individual weighed 165 pounds and never sick except a year before when he developed an axillary lymphadenitis following a scratch of a finger His father died at eighty-six years—cause unknown his mother at fifty of diabetes Two brothers and three sisters wife and six children were living and well. By occupation he was a buyer in the commission market and his work was responsible for occasional exposure to inclement weather

Physical examination revealed a well nourished white male about fifty years of age who did not appear acutely ill but presented a definite icteric tinge of his skin and sclera when observed on the day following the second acute attack. Aside from moderate tenderness in his right flank the remainder of the physical examination was without interest

The patient was asked to enter the hospital and on the morning of his admission he had another acute attack. He passed a reddish brown urine which was reported by the laboratory as positive for albumin and strongly positive for blood Blood-count that day revealed 3 720 000 red blood-corpuscles 9750 white blood-corpuscles 80 per cent. hemoglobin and a differential count of 31 small lymphocytes and 69 polymorphonuclear neutrophils.

A cystoscope was passed and a pyelogram made of each kidney The pyelogram made of the left kidney was entirely normal while that of the right revealed an absence of the entire lower calyx Difficulty in the cystoscopy was encountered owing to the oozing of blood from the right ureteral orifice, which, however, might have been traumatic

He was seen in consultation by several excellent men who concurred in the diagnosis of a neoplasm of right kidney, possibly a hypernephroma, and advised surgical exploration A right kidney incision exposed an apparently normal kidney in size and shape, which on opening the kidney pelvis revealed a congenital absence of the lower calyx, but no calculi or tumor tissue The organ was left in situ and the wound closed, the surgeon suggested a diagnosis of essential hematuria Recovery from the operation was uneventful and the patient left the hospital after two weeks' and remained confined to his home for another two weeks On his first day out doors he was seized with another acute attack. I obtained the urine and examined the fresh specimen myself For the first time I was struck by the reddish-brown urine which gave a strongly positive benzidine reaction, but contained almost no red blood-corpuscles Suspecting a hemoglobinuria, I sent in blood smears for plasmodium examination, and ordered a Wassermann test Examination for the plasmodium was negative, but the Wassermann and Kahn tests were returned four plus It was then obvious that the condition was that of paroxysmal hemoglobinuria brought on by cold in a syphilitic person

It is interesting to note that during the past thirty years, among some 156,000 ward patients treated at the Massachusetts General Hospital, there have been but 9 cases of paroxysmal hemoglobinuria I have been unable to find a report of a previous case from Chicago Two important factors influence its occurrence in the syphilitic patient (1) Inadequate or no antisyphilitic treatment, (2) exposure to temperature low enough to initiate paroxysms

The differential diagnosis includes hematuria, due to renal calculus or malignancy, hematoporphyrinuria, due to the administration of sulphonal or trional, malarial hemoglobinuria, Mickel's epidemic hemoglobinuria of the new-born, Raynaud's disease, and hemoglobinuria following the administration of drugs, such as potassium chlorate, naphthol and pyrogallol, or the inhalation of carbon monoxid, carbon bisulphid, or naphtha vapor No evidence of a spontaneous cure can be found in the literature, but under antisyphilitic treatment the symptoms of the disease usually disappear

The patient was then referred to Dr Pilot to corroborate

and prove the diagnosis by further investigation In our opinion the condition is more prevalent than the literature leads us to believe One of us (Dr F) has since discovered another case in a congenitally luetic boy five years old, who had recurrent attacks during the fall and winter for three successive years, and the case had been considered one of essential hematuria

Discussion by Dr Pilot.—When I first saw the patient he was free from symptoms and from the history and the observations by Dr Friedman, the condition appeared to be typical of paroxysmal hemoglobinuria A peculiar phenomenon of this clinical state, which has been the subject of investigations by Landsteiner and others was demonstrated in this case Blood was drawn from the vein and then placed in the refrigerator for ten minutes On removal of the specimen to room temperature the serum assumed the transparent reddish hue typical of hemolyzed blood A hemolysin is present in the blood plasma of these individuals which is activated by changes in temperature, particularly by exposure to cold and then to room temperature. The hemolysis can be carried out in the test tube as it is in the patient when he is exposed to cold weather or by purposely immersing the hand or foot in a pan of very cold water In the patient a hemoglobinemia is produced and the hemoglobin passes through the kidney, giving to the urine the reddish transparent color characteristic of hemoglobinuria During the hemoglobinemia symptoms often result from the toxic action of the liberated hemoglobin

By instituting antisyphilitic treatment the condition can be improved or cured This patient after 3 doses of 0 45 neosalvarsan had one attack in very cold weather Owing to reactions the dosage was reduced to 0 15 gm for 5 doses and only one slight attack occurred after exposure to cold Since that time he has received small doses of neosalvarsan, together with mercury and iodids and no recurrence has taken place The Wassermann and Kahn tests, however, remain strongly positive and the hemolytic test still demonstrable

CLINIC OF DR G K PENN

ST LUKE'S HOSPITAL

THE USE OF DIGITALIS IN THE CONTROL OF AURICULAR FIBRILLATION

SIR JAMES MACKENZIE,[1] in his text book, Diseases of the Heart, stated that 60 to 70 per cent of the cases of heart failure met with in practice owed their failure directly to fibrillation of the auricles, or had the failure aggravated by its presence Perhaps these figures are somewhat high, but they serve to show the importance of auricular fibrillation as a cause of heart failure

It would be pleasing indeed if every case of heart failure showing auricular fibrillation might have the cardiac insufficiency entirely removed by the satisfactory control of the arrhythmia Unfortunately, such results cannot be obtained, but we believe that in the vast majority of such cases the disability imposed by the arrhythmia itself may be largely abolished

Auricular fibrillation may occur in connection with many forms of heart disease, and it may occur without disease of the heart at all. Let us consider for a moment that auricular fibrillation is not a disease of the heart Let us say it is a disorder of the heart, a disorder of the heart that may render the cardiac function totally inadequate to maintain the sufferer from it in comfort, or, more important, in a useful occupation Let us remember that the disability caused by this disorder is entirely independent of the structural integrity of the heart The disability of auricular fibrillation is caused largely by the exceedingly rapid ventricular rate and the resulting inadequacy of individual contractions of the ventricle When the ventricular rate has been properly retarded, and the individual contractions made

more effective thereby, then the disability caused by the arrhythmia itself is greatly benefited

With this disorder brought under control, and the disability caused by it largely removed, the activity of the patient is then determined by the amount of cardiac disease or damage that is present Those who have little or moderate cardiac damage will have little or moderate restriction of activity, although they may have been completely disabled by the presence of an uncontrolled complete arrhythmia of the heart Thus, we see the importance of controlling the disability imposed by auricular fibrillation

This morning we shall discuss the use of digitalis in the control of this disorder The patients you see here are all under digitalis control We shall not consider quinidin at this time because, with the restoration of a sinus rhythm, we are no longer dealing with fibrillation and there are many cases that do not yield to quinidin or to whom we do not wish to administer it

It is probable that the most striking therapeutic results obtained by the use of digitalis since its introduction into medicine by Withering have been seen in auricular fibrillation Cushny states that some of Withering's best cases showed this arrhythmia, although, of course, Withering knew nothing about this curious phenomenon known then as *pulsus irregularis perpetuus*

During the century following the introduction of digitalis little progress was made in its use Throughout the nineteenth century, Cushny[2] states, "the physician continued to prescribe digitalis in diseases of the heart after the manner of his father, and perhaps with less discrimination than his grandfather" Indeed, little may be added, even today, to Withering s original instructions governing its use[3] Every one who prescribes digitalis might read with profit his original article

It is only during the first years of the present century that digitalis therapy in auricular fibrillation began to move to its present position It was not until 1906 that the first case of auricular fibrillation in the human being was described as such by Cushny and Edmunds,[4] and it was not until 1909 that elec-

trocardiographic methods in the hands of Rothberg and Winterberger and Lewis proved that auricular fibrillation was a disease of frequent occurrence in the human heart

It was the work of Cushny and his students on the action of digitalis correlated with the clinical observations of Mackenzie and Wenkebach and their students that digitalis therapy was placed on its present plane, and its specific action in auricular fibrillation pointed out

This is not the proper place to enter into a discussion of the action of digitalis on the heart, but a few words relative to its action in complete arrhythmia are necessary for a good understanding of its use

It is, I believe, conceded by all that the specific action in auricular fibrillation is that of decreasing the conductivity between the auricles and ventricles, thereby slowing the ventricular rate The cause of the decrease in conductivity is probably a two fold one There is depression due to vagus stimulation and depression due to direct action on the conducting tissues The relative importance of vagus inhibition and direct action has been a subject of some controversy that need not be discussed here, but which may serve to explain the long-continued improvement in a few cases after digitalis has been discontinued

Further, it seems necessary to procure an adequate concentration of digitalis in the tissues before proper control is obtained and when this concentration is attained, it is necessary to give a sufficient dose to make up for daily excretion and maintain the proper concentration in the tissues

Lastly, it is usually necessary to continue the digitalis as long as the patient continues to fibrillate and that, ordinarily, is as long as he lives

The statements made in this discussion are the result of a study of material taken from the hospital Medical Service and Out Patient Department and from private practice The period of observation extends from 1917 to the present time Only those patients were studied who are still under observation or who remained under observation until the time of their death Incidentally, no patient in this group died from heart failure

due to auricular fibrillation Many have succumbed to heart disease, to recurrent cardiac infection, to coronary accidents, and to causes other than heart disease, but in no case where the arrhythmia had been brought under control could the death be attributed to heart failure due to auricular fibrillation

Each patient who showed definite signs of decompensation was rapidly digitalized When the patient was hospitalized and under close observation and had not had digitalis recently, large doses were given, following the suggestion of Eggleston [6] Doses of 0 75 gram the first day followed by a like or slightly less dose on subsequent days were not uncommon In this way rapid digitalization is brought about The indications of the digitalis effect are the increased urinary output, the recession of the swollen liver, the disappearance of fluid from the tissues and the serous cavities, and the slowing of the pulse-rate with a decrease of the pulse deficit The appearance of premature beats of ventricular origin, coupling, or the onset of nausea indicate that the optimum point has been slightly exceeded When the electrocardiogram is available, the appearance of frequent premature beats of ventricular origin indicates a good digitalis concentration In the same manner, the depression of a previously high T wave is probably of some value While not wishing to detract from the value of the electrocardiogram as a guide in this matter, I may safely say that one can get along very well without it

The majority of patients in this group, however, were ambulatory and it was not considered necessary to hospitalize them They presented themselves for examination, showing only a moderate degree of cardiac insufficiency The chief complaint was great dyspnea and palpitation of the heart on exertion Such patients were usually allowed to go about their customary occupation, if such occupation was suitable, or, at most, were sent home to rest while control was being established Digitalis was administered in somewhat smaller doses than in the hospitalized group, and the optimum concentration reached more slowly Doses of 0 4 gram to 0 5 gram daily for five days to a week usually brought about the desired result

In every case the digitalis was given by mouth We believe it is rarely necessary to give it otherwise One often hears that the stomach will not tolerate digitalis We have never found that a compressed tablet of powdered leaf added anything in the way of gastro intestinal irritation

The intramuscular injection of digitalis produces its effect slightly more rapidly than does the administration of adequate amounts by mouth, but it is doubtful that the slightly lessened time constitutes a clinical advantage of any moment and we believe that the indications for intravenous injection are very rare indeed

The preparation used in most cases was powdered leaf, either a compressed tablet or a capsule I do not believe that this form of digitalis possesses any superiority in action over other good preparations, but it has the advantage of easier and more accurate measurement and it is more easily carried about The measurement of drops and the conversion of drops into minims is a bothersome task and leaves something to be desired in the way of accuracy Also, this procedure constitutes a severe strain on the mental capacity of many patients in the Out-Patient Department We find that the less difficulty that surrounds the administration of a drug the more faithfully the patient follows direction

One often sees a patient with auricular fibrillation who complains of little discomfort with an uncontrolled heart rate in the neighborhood of 120 to 130 per minute While such patients may be up and about and even do a fair amount of work under such conditions, we have invariably found that they are better and more comfortable when the heart rate is brought within more reasonable limits by digitalis

Occasionally, one sees a patient with auricular fibrillation and a normal or even low pulse rate Such patients are not benefited by digitalis and may even be harmed by its use

After the patient is brought under satisfactory control, a daily dose of digitalis is necessary to maintain the proper concentration in the tissues This daily dose varies from patient to patient, and is apparently dependent upon the excretion rate

of each patient We have found the average daily dose to be approximately the equivalent of 0 2 gram of powdered leaf Some patients require 0 4 gram, others do well on less than 0 06 gram We have discovered no way of predicting the daily dose The usual procedure is to start with the average daily dose and vary it with one or the other as the occasion demands When the correct dose is determined, it often remains constant for months, and even years Sometimes it is necessary to gradually vary the dose one way or the other, as in one patient who, in 1921, did well on a daily dose of 0 1 gram and in 1928 required 0 4 gram to maintain comfort, or another who, in 1924, required 0 2 gram and now received 0 05 gram

Occasionally, a rather curious phenomenon is encountered in which a patient who has gone for months on the same dose suddenly begins to exhibit signs of failure while constantly taking the same amount of digitalis that previously kept him quite comfortable If such a patient shows no sign of intercurrent acute infection, a recurrent attack of heart disease, an exacerbation of thyroidism, or some other underlying cause, we merely increase the daily dose until he is once more under satisfactory control, and then it is usually possible to drop back to the original amount

It is probably impossible and is certainly unwise to set any any definite standards for proper control The general comfort of the patient is the best guide Some patients do well with the pulse between 60 and 70, others complain of discomfort if the pulse falls below 90

The pulse deficit is a matter of some importance In the uncontrolled case, the apical rate may be 150 or 160 or even more, with a radial rate of 40 to 50 As the patient is brought under control these two rates approach each other and may become identical I do not believe it is necessary to strive to make them identical and not infrequently it is unwise to completely abolish the pulse deficit A pulse deficit of 6 to 8 per minute was present in most of our cases, and I have never seen a patient who was made more comfortable by the abolition of this small deficit

On the contrary, I have seen a number of patients who complained sharply of discomfort if the deficit fell below 15 to 20 per minute Again the general comfort of the patient is the best guide

Many patients have attained a high degree of proficiency in regulating their own digitalis dosage They have come to recognize certain signs that indicate overdosage or underdosage in their own particular case Some have been taught to use the stethoscope to count the apical rate and to compute the pulse deficit Such information in the hands of the patient is of great value in the successful control, but before imparting this knowledge to the patient his intelligence and nervous stability must be carefully assessed

The subject should not be left without a word as to its economic significance, and it is largely to emphasize the importance of this point that I am bringing these patients before you A number of patients have been rescued from destitution and restored to economic independence by the control of auricular fibrillation With the prospect of many years of life before him the difference between invalidism and the ability to work is a very important one in the case of the sufferer from auricular fibrillation And just this difference is often dependent upon a proper digitalis control

Case I.—The first patient is F V forty nine years old a laborer He came under my observation in 1917 He has rheumatic carditis with mitral disease and auricular fibrillation The fibrillation was present when he first came under observation and I am unable to determine the time at which it first appeared When first observed he was badly decompensated and unable to work. He was hospitalized and the arrhythmia brought under control He has taken digitalis continuously for the past twelve years The average daily dose has been 0 1 gram. Occasionally he seems to require 0 2 gram for a few weeks and occasionally the dose is dropped to 0 05 gram for a time The apical pulse today is 78 and the radial 69 This patient has lost no time from work since 1917 because of cardiac decompensation He was hospitalized in 1922 and given quinidin in an attempt to restore normal sinus rhythm. The attempt was not successful

He was hospitalized again in 1926 because of an acute bronchitis He had been away from work on several occasions with respiratory tract infection but has had no severe heart failure. Three times during the past twelve years he has slipped out of control while taking his usual amount of digitalis.

The first time he came in with an apical rate of 140 and a radial rate that was in the neighborhood of 60 He had a swollen liver and a moderate degree of dyspnea No definite cause for this phenomenon could be discovered so he was allowed to go about his business, but the digitalis was increased to 0 4 gram daily for forty-eight days, after which it was possible to reduce it to the previous dose of 0 1 gram daily The two subsequent slips were identical with the first in all essential particulars At the present time, he is taking 0 05 gram daily, and is continuously engaged in his usual work of sweeping steel shavings from the floor in one of the steel mills

Case II —This patient, Mrs L F , is thirty-seven years old and has rheumatic carditis, with mitral disease, and auricular fibrillation She first came under observation in 1919 because of her heart disease which had already been present a number of years In 1919 she had a normal sinus rhythm. She went to Florida in November, 1921 and did not return until September, 1923 When I saw her in 1923 the auricles were in fibrillation, and the heart was moderately decompensated She was immediately hospitalized and the arrhythmia was brought under control She was discharged from the hospital on a daily dose of 0 2 gram of digitalis In February, 1924 her pulse was found to be 64/60 and 66/64 on two examinations She seemed to be in good condition, but complained of tiring rather easily and she had some pre cordial pain The digitalis was reduced to 0 1 gram daily, the pulse rate increased to 90/80, and remained constantly in about that neighborhood The discomfort immediately disappeared and she has had no occasion to alter the digitalis dose since 1924 In March of that year, she had whooping-cough, but made a good recovery At present she is engaged in her usual household duties, is perfectly compensated, and is quite comfortable

Case III —This boy, K K., presents a somewhat different picture He is now twenty-two years of age He came in first five years ago, when he was seventeen He has had heart disease since he was seven There were repeated recurrences, and at the time he first came under observation here, his heart was very badly damaged indeed He has rheumatic carditis and mitral disease, adherent pericardium, and auricular fibrillation The heart by x-ray occupies 78 per cent of the thoracic diameter Even without the added hindrance of auricular fibrillation, one would be justified in suspecting that there would be but little reserve left in this heart And this boy has not done as well as some of the others But the important point is that the auricular fibrillation has not been a handicap He had done just as well as anyone with a comparable heart without auricular fibrillation He has been employed during a large part of the past five years and a considerable part of his unemployment has been due to the fact that he was unable to find suitable work. His biggest trouble has been the frequent occurrence of respiratory tract infections

Another interesting thing about this boy is the fact that he gets along on very small doses of digitalis In view of the extensive damage in this heart, it seems a fair inference that the damage has involved the conducting tissues This brings about some difficulty in the transmission of impulses from the

auricle to the ventricle o partial block If you wish In other words we have a digitalis-like effect in the conducting tissue without the use of digitalis. Now when this boy is ot rest he does very well without ony digitolis In 1927 he was in the hospital four months os the result of a bronchopneumonia During the last three months of his hospital residence he received no digitalis at all, and his pulse remained between 70 and 80 with little or no deficit

However when he is up and about and taking moderate exercise the pulse-rate accelerates and o deficit becomes evident This boy is not com fortable when his pulse exceeds 90 so it is necessary to give him digitalis at such times to promote the greatest cardiac efficiency—0 05 gram daily does the work. For the past six months he has been engaged as clerk in a drug store

Case IV —Mrs. B is forty seven years of age She came under observa tion in 192. She had been totally disabled for several months because of dyspnea and edema. She was found to have mitral disease ond auricular fibrillation. The pulse on odmission was 140/120 The fibrillation was brought under control, and the disability promptly cleared up. She left the hospital in one month taking a daily dose of 0 2 gram of digitalis. The dose has not been changed there has been no further discomfort ond she is following her occupation of designing frocks

Case V —If you will bear with me o few moments longer I should like to read from the record of J S He came to us in 1921 We could obtain no history of heart disease prior to 1918 In 1918 he had a severe attack of in fluenza from which he never completely recovered He stated that his heart was irregular following the influenzal attack and that he had no knowledge of any disease of the heart preceding it His cardiac function seemed so poor that he had been entered in the Home for Incurables. He was sent to us from the Home because he seemed to be in very dangerous condition from heart failure. He was found to have mitral disease and auricular fibrillation He was kept in the hospital for two months in 1921 during which time his ar rhythmia was brought under control and his cardiac function improved enormously He was discharged from the hospital and returned in a few weeks when an effort was made to restore normal sinus rhythm by the use of quinidin. The attempt failed and he was sent out under digitalis control and told to get a job He worked continuously from the fall of 1921 until his death in 1928 first as an errand boy then as a hotel clerk and cashier

In February 1925 he underwent an operation for a gangrenous appendix. His recovery was uneventful. Curiously enough it was found necessary to gradually increase his digitalis dose. In 1921 he did very well on 0 1 gram daily while in 1928 0 4 gram was necessary for comfort He was most comfortable when the apical pulse was in the neighborhood of 90 On one occasion while trying a new digitalis preparation I produced a complete block with a regular rate of 60 and no deficit. He immediately protested and it was necessary to withdraw the digitalis until the pulse had come back to its usual level. In February 1928 he succumbed to a bronchopneumonia.

The type of occupation is of some importance, but certainly those who are equipped to do work that comes within their cardiac limits need suffer no handicap because of auricular fibrillation Given a fairly good heart muscle, a modicum of patience and intelligence, and the patient with auricular fibrillation can be kept at work until he dies from some cause other than fibrillation

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CLINIC OF DR JAMES H HUTTON

WOODLAWN CLINIC AND HOSPITAL

THREE ILLUSTRATIVE CASES OF ENDOCRINE DISORDER

In the minds of many medical men there is a resistance to the diagnosis of any endocrine disorder Men overlook or forget the fact that these glands are an intimate part of the body, that many of them are necessary to life, and that others differentiate us from vegetative organisms and add materially to our joy in life The evidence at hand indicates that they are influenced by infection, by traumatism, either emotional or physical, in the same way and to the same extent as other organs In discussing other syndromes we are told that a diganosis should be made early, in the very incipience of the disease, but in endocrine disorders the major portion of the profession takes the stand that a diagnosis should be made only when the case is so well marked, of such severe degree, or so far advanced that there is no likelihood of mistake and almost as little likelihood of improving the condition by treatment

An erroneous idea abounds that endocrine disorders occur with such rarity that the average doctor seldom sees one, and that when they do occur, they mark their victims by some unusual physical or mental characteristics that set them apart from their fellows

Since these structures are influenced by infection, trauma or dietary indiscretion the same as are other structures of the body, disorders of these glands are naturally amenable to the same rules of treatment and prognosis as are disorders of other organs, that is, the earlier endocrine disorders are recognized, the more

promptly and vigorously they are treated, the better the outlook for their ultimate relief

That much remains to be discovered regarding the function of these organs and that preparations of them to be used in treatment are not ideal or not so good as they are likely to be in future years, goes without saying, but this is no good reason for refusing to use the knowledge and material at hand for the relief of suffering This is the spirit which prompts me to cite the following cases

Case I —Miss L , aged seventeen, came under observation April 14, 1929 Her complaints were

1 Vasomotor rhinitis and bronchitis
2 Irregularity of the menstrual periods
3 Obesity

Past History —Her past history showed that she had a severe bronchitis at age ten which lasted several weeks She had hay-fever in the summer of 1928, since which time she apparently has had vasomotor rhinitis She admitted eating a great deal of meat, fish, and eggs, considerable bread, pastries, candy, etc , with very little fruit and green vegetables She slept well, her bowels were regular

The menstrual periods began at age twelve, were always irregular, the intervals varying from one to three months Lately they were two or three months apart The duration was five days, the flow moderate, and the pain slight

Family History —Family history was unimportant except that her father and mother are both below average height, being little above 5 feet, and the father especially is inclined to the pituitary type of obesity

Developmental History —She weighed 8½ pounds at birth There were no injuries at birth She got her first tooth at eight months, and walked at nine months, and was said to have been anemic up to the age of six or seven When her tonsils and adenoids were removed at the age of six, she weighed 40 pounds, at age seven, 40 pounds, at age eight, 60 pounds, at age thirteen, 140 pounds, at age seventeen, when she came under my observation, she weighed 173½ pounds

Physical Examination —Temperature 98° F , blood-pressure 110/80, height, 61¼ inches, weight 173½ pounds

She was a fat, blonde girl, having coarse heavy hair, heavy brows, and a luxurious growth of axillary and pubic hair The pubic hair was of the male type of distribution The skin was quite rough and coarse, especially on the outer aspects of the arms The teeth were even, regular, and evidently of fair quality The nails were small, but otherwise negative The face was full and round, with a double chin The thyroid was of normal size There were no palpable glands There was marked padding on the dorsum of the hands and feet, about the wrists, and in the dorsal cervical region, with marked

folds on the lateral aspects of the thorax. The abdomen was of the pituitary type having four folds it was otherwise negative The heart and lungs were free of any adventitious sounds or signs of pathology The palpebral fissures were narrow the eyes were otherwise entirely negative. The nose was small and of the pituitary type. It was apparently otherwise negative

Laboratory—Basal metabolic rate minus 1 7 per cent The Goetsch test showed a negative response to adrenalin The urine was of high specific gravity but otherwise normal It contained 9.3 grams of chlorids per twenty four hours.

Blood chemistry Sugar 72 mg per 100 c.c. of blood Calcium 10 0 mg per 100 c.c. of blood Uric acid 3 0 mg per 100 c.c of blood Cholesterol, 241 mg per 100 c.c. of blood

The Wassermann was negative on the blood

Blood-count showed Hemoglobin, 84 per cent. red blood-cells 4 600 000 white blood-cells 8960 polymorphonuclears 73 lymphocytes 24 large monocytes, 1 neutrophilic myelocytes 1 eosinophilic myelocytes 1 basophils, 1 alveolar CO_2 32 43 volumes per cent. Her galactose tolerance was above 40 grams. The feces were entirely negative

Diagnosis—On the basis of her fat distribution the normal basal metabolic rate the galactose tolerance ond irregular menstrual periods short stature, and typical hands a diagnosis was made of hypopituitarism of the bibobar type, and secondary to this ovarian insufficiency

Treatment—She was given by mouth ovarian residue 5 grains t i d and whole pituitary grains 3, t. i. d and was put on o restricted diet she was also given calcium lactate for her vasomotor rhinitis By June 5th she weighed 165 pounds. From then until July 17th she was given at intervals of three or four days subcutaneous injections of pituitrin ½ c.c. and ovarian residue 1 c.c. At that time she weighed 149½ pounds. Her skin was much smoother her periods were occurring regularly every two months. On August 10th her pulse was 100 blood pressure 105/70 weight 140 pounds She was listless easily tired out, no pep generally discouraged. She admitted having been on the "eighteen-day diet. August 26th weight 141½ pounds pulse 78 the last period was only ten days late The periods were regular in September and October September 20th pulse 100 blood pressure 115/70 weight 141½ pounds, she had no treatment and had been on n liberal diet November 4th, pulse 80 weight 137½ pounds, the last period was reported to have been on time. She was feeling quite well and was doing well in the University Her skin was quite smooth and of normal texture Her vasomotor rhinitis had disappeared. During this period of observation she has occasionally stopped hypodermic medication for a month or so During such times her loss in weight was slower or stopped entirely

Case II. Parathyroid Tetany—Mrs G aged fifty five had a subtotal thyroidectomy May 15 1928 She complained of much numbness and tingling of the extremities with some apprehension the day following the operation By the fifth postoperative day she presented well marked signs of tetany

When I first saw her on June 10 1928 she was in a severe tetanic convulsion all of the extremities being involved. She was immediately given

calcium lactate, 1 dram t i d , gluco calcium 10 c c intravenously, and 20 units of parathormone daily Meat was entirely stricken from her diet and she was put on a very low protein intake Her most urgent symptoms promptly disappeared and she made a slow partial recovery

Past History—The goiter had been present since puberty The date of onset of toxic symptoms was uncertain Mild exophthalmos was present prior to operation During the past five years she had had considerable rheumatism in her ankles, knees, legs, and wrists Pelvic peritonitis occurred soon after marriage, apparently accompanying a miscarriage She had had much tonsillitis until the tonsils were removed by diathermy two years before the thyroidectomy

Family History—Was negative except that her mother and one sister had had goiters The patient had had three miscarriages

Menstrual history was unimportant

On August 5, 1928 she began to experience a feeling of numbness and tingling of the extremities and apprehension, later cramps occurred, and finally tetanic contractions on August 8th These symptoms occurred after she had been using considerable meat They were promptly relieved after the administration of gluco calcium intravenously By August 12th she was able to be up and reported at the office At that time her complaints were

1 That her ankles were lame, pained a good deal, had been tender since the convulsion of August 8th Her knees also caused her some pain and were somewhat stiff

2 There was much gas and belching and she had had a good deal of heartburn lately this occurred from one to three hours after meals, and was only occasionally relieved by soda She had experienced this trouble for a good many years

3 What she described as "nervous spells," a sensation of coldness began at her feet, traveled to her head, with tingling over her entire body She stated that she felt as if she were "about to pass out" if she closed her eyes There was a good deal of apprehension and occasionally black spots before her eyes These symptoms began shortly after the operation and had been present at various times ever since

4 Hot flashes These had been present at intervals for years, but had been much worse since the operation

5 She was cold and clammy all of the time

6 There was some precordial pain, but she complained more of palpitation and throbbing So far as she knew, there had been no irregularity of the heart There was no detectable irregularity, no enlargement, and no murmurs

On August 14th her basal metabolic rate was minus 15 per cent , pulse 66, respiration 16, weight 139 pounds Treatment at this time consisted of calcium lactate with 20 units of paroidin on alternate days She was allowed one egg daily and meat on alternate days She was also given thyroid ½ grain daily

Thyroid was administered because it is well known that it sometimes seems to act as an adjuvant to the parathyroid hormone in promoting the assimilation of calcium About this time she began taking radiation from the

Quartz lamp The parathyroid hormone was omitted every fifth day when she was given ovarian residue subcutaneously with a view to relieving her hot flashes which were becoming quite annoying This was later discontinued as it seemed to aggravate rather than to alleviate the hot flashes. The ultra violet radiations seemed to have no beneficial effect They were taken at home without supervision Later tests seemed to prove that ultraviolet rays were scarce or entirely absent from the apparatus she was using. In September she made a long automobile trip and indulged in a good deal of social activities after which she complained of numbness and tingling considerable depression and apprehension By the latter part of October she was enjoying fair health She continued to gain weight slowly from 139 pounds, August 14 1928 to 153 pounds December 27 1928

She was definitely worse after taking considerable meat after unusual excitement or muscular exertion Her complaints were usually numbness and tingling pain in her limbs rather than in her joints and throbbing of her heart. The parathyroid hormone was increased or decreased as indicated by her complaints. For a while she got along on 20 units daily by the first of January 1929 she was taking 20 units twice a day While she felt generally much better her sleep was still disturbed by the throbbing January 9 1929 she fell and bruised her side after which her nervous symptoms became more pronounced She complained of being cold all of the time and of being somewhat somnolent her pulse was 66 She was again given thyroid 1 grain per day By February 20 1929 her weight had increased to 156 pounds and the pain in her extremities was the most troublesome complaint She was taking 20 units of paroidin one day and 40 the next. By March 6th it was necessary to increase this to 40 units daily March 29th she complained of severe pain in her knees and ankles that her legs were very cold that her hands and feet frequently went to sleep She was given cod liver oil in the hope that this might influence the calcium metabolism favorably

April 12 1929 She reported being considerably upset by cod liver oil so it was stopped.

April 22 1929 Blood pressure 150/95—a systolic murmur was heard at the apex. Her condition gradually became worse and on May 6 1929 the parathormone was continued at 20 units twice a day She continued to have some diarrhea which had begun some weeks ago Each movement was preceded by many bizarre nervous sensations On May 27 1929 her blood sugar was found to be only 65 mg She was directed to take more sweets which action relieved many of her symptoms. On May 29th the paroidin was increased to 30 units twice a day June 5 1929 she reported that the aching and pain in the legs promptly disappeared after the dose of paroidin was increased.

June 20th weight 160 pounds pulse 76 She reported that she had been feeling very well until the recurrence of diarrhea when the throbbing again became troublesome.

July 17th. She was feeling very well so the paroidin was reduced to 50 units per day

July 22d She reported not feeling so well as her sleep was disturbed because she was so cold and she was feeling generally upset. However she

improved after a few days and the paroidin was reduced to 40 units daily on August 8th

August 19th She reported having been under considerable mental and physical strain She was nervous, complained of much throbbing, and stated that her hands and feet were asleep Pulse 78, blood-pressure 120/80 She was ordered to take more rest, crowd liquids, and was given acterol (irradiated engosterol) The dosage of paroidin was not changed, as it was hoped the acterol would reinforce the action of it

August 22d She was much more nervous and reported some cramps and pain in her legs and joints These symptoms were promptly relieved by adding 20 units of paroidin as an extra dose The acterol seemed to definitely upset her and make her feel generally worse During its administration it was necessary to increase the paroidin to 70 units per day Her weight had increased to 163½ pounds We were unable to reduce the dose of parathyroid without the recurrence of most of her disagreeable complaints The acterol was discontinued on September 11th On October 1st she reported that she began feeling better very soon after the acterol was discontinued She was now taking only 45 units of paroidin per day

October 24th She reported that she had discontinued eating any meat but chicken and fish For some curious reason patients seem to regard chicken and fish as not being meat The paroidin had been reduced to 40 units per day Her basal metabolic rate was minus 7 per cent The course of her blood-calcium is indicated in the table

June 18, 1928	Calcium 10 5
July 6, 1928	Non-protein nitrogen 24
July 6, 1928	Calcium 9 35
July 6, 1928	Uric acid 3 1
July 16, 1928	Calcium 9 8
August 11, 1928	Calcium 10 6
August 20, 1928	Calcium 7 9
October 1, 1928	Sugar 100
October 1, 1928	Calcium 8 9
October 1, 1928	Uric acid 4
July 28, 1929	Sugar 65
July 28, 1929	Calcium 8
July 28, 1929	Uric acid 3 4
November 1, 1929	Calcium 8 5

Some years ago Dragsted proved that the parathyroids are intimately concerned with the toxins arising from bacterial proteolysis in the bowel Lately we seem to have forgotten this fact, and have centered our attention on the relation of the parathyroids to calcium metabolism, especially the level of the serum calcium, which probably is not an accurate measure of the level of the blood calcium It was also shown by Dragsted

and Luckhart that muscular exercise, pregnancy, and the menstrual periods have considerable influence on the parathyroids

Several times it has been found that the use of the parathyroid hormone in considerable doses has little effect on the serum calcium unless small doses of thyroid are administered In this patient no trophic disturbances occurred except a considerable loss of hair No changes were noticed in the nails or teeth, and none in the skin except clamminess and coldness It is quite likely that patients are influenced quite as much by the rapidity of the fall in the blood calcium as they are by its extent For example, tetanic twitchings or convulsions occur if the calcium falls from a normal level of 10 or 12 mg, before operation to a level of 6 or 7 immediately after an operation But one not infrequently finds a level of 6 mg in ambulatory patients who show no signs of tetany

The instructive features of this case are

1 The larger doses of parathyroid hormone that are necessary now as compared with those required in the beginning

2 The persistence of symptoms in spite of the practically normal blood calcium

3 The relation of the symptoms to diet She was always worse after taking a heavy protein diet and was quickly relieved of many disagreeable symptoms when her carbohydrate intake was increased on finding her blood-sugar so low

4 The symptoms were aggravated by heavy protein diet, by exercise, muscular activity, emotional strain, and trauma

5 This emphasizes the importance of the functions of the parathyroids other than the maintenance of the blood calcium at the proper level.

Parathormone and paroidin refer to the parathyroid hormone preparations They alternated in the patient's favor, she sometimes preferred one and again the other

Case III. Ovarian Insufficiency —Miss S aged twenty-seven came under observation October 27 1928. She complained of

1. Dysmenorrhea. The pain began when the flow started and lasted throughout the first day it was quite severe and was accompanied by a great deal of nausea and vomiting

2 She was tired and easily exhausted This dated from an abortion in October, 1927, and the dysmenorrhea had been much worse since that event

3 She is sensitive to cold and always has cold hands and feet

4 Loss of weight She lost considerable weight after an appendectomy seven years ago, her weight dropping from 140 to 125 pounds, and has recently dropped to 120 pounds Her appetite was poor, she was seminauseated by food She slept fairly well and her bowels were regular

Past History—Appendectomy seven years ago, several abscessed teeth extracted early in 1928 This was accompanied by severe hemorrhages, necessitating the use of a hemostatic serum

Menstrual History—The periods began at thirteen They had always been painful, although not sufficiently so to keep her from school or work Pain has been much worse since miscarriage in October, 1927 The flow was profuse, lasting seven days with a great many clots Lately the pain had been so severe that she frequently fainted This had been especially marked in the past year

Family and *developmental history* was negative

Physical Examination—Temperature 97° F, pulse 80, blood-pressure 110/70

Height 5 feet, 7½ inches, with rather long arms and legs, and long tapering hands and fingers There were no abnormal findings in the chest or abdomen Examination of the nervous system revealed no abnormalities The hair suit was unusual in that there was some present on the chest and about the nipples The pubic hair was of the male type of distribution Vaginal examination revealed no abnormalities Some of the teeth looked suspicious Her basal metabolic rate was minus 5 per cent Her blood-count was as follows

Hemoglobin 85 per cent, red blood cells 4,870,000, white blood cells 10,700, polymorphonuclears 44 per cent, lymphocytes 39, large monocytes 4, eosinophils 13

The large number of lymphocytes and eosinophils is significant, as ovarian disturbances are believed to be accompanied by an increase in the eosinophils Blood-calcium 8 6 mg The urine was negative Blood Wassermann was negative

On the basis of the history, the stature, the blood-count, and hair distribution and the absence of any other condition to account for her trouble, a diagnosis was made of ovarian insufficiency She was given ovarian residue 5 grains, t i d, and 1 ampule subcutaneously every three days November 19th she reported that her period was on time, entirely free from pain, without vomiting, and that that was the first painless period she had ever experienced She had also gained 2 pounds Later she was given estrogen, 1 ampule twice a week. This seemed to work no better than the ovarian residue, so the latter was used Her periods continued to be free from pain and without nausea and vomiting

June 21, 1929 She reported that her periods were regular and free from pain, nausea, and vomiting, her weight had increased to 135 pounds Subjectively, she reported feeling better than she had for many years

In that case, as in many others, the diagnosis of ovarian insufficiency was based on the history, the rather meager physical and laboratory findings, and the exclusion of any other condition as a causative factor in the patient's complaints The correctness of the diagnosis seems to have been substantiated by the results of treatment

CLINIC OF DR AARON ARKIN

Cook County Hospital

BRONCHUS CARCINOMA

Bronchus carcinoma can no longer be considered a rare disease. In large European clinics, where autopsies are performed on all fatal cases, this disease has been recognized for years About twenty years ago most of the cases were diagnosed by the pathologist, the clinician failed to recognize the clinical symptoms With the aid of the roentgenologist, the clinician should today be able to diagnose at least four fifths of all cases, and to suspect the disease in the other one-fifth As we shall see, certain types are quite easy to diagnose clinically, other forms only by x ray examination Bronchography and bronchoscopy, artificial pneumothorax, biopsy, and microscopic examination of exudates are aids in the recognition of some cases In the last ten years a number of contributions to the literature of the disease have been made in this country

Frequency of Bronchus Carcinoma.—Bronchus carcinoma has increased in many countries in the past ten years This increase is not alone due to better diagnosis, as the pathologic institutes in which this disease has been recognized for years also register a marked increase in the number of cases The increase has been greatest in Germany, the United States, Austria, and Switzerland, with little or no increase in the Scandinavian countries. Ten years ago bronchus carcinoma constituted about 2 per cent of all carcinomas, today it has risen to about 7 per cent Some writers report as high as 10 per cent Bronchus carcinoma is most frequent in persons from forty to sixty years of age, the largest number occurring from forty to fifty The ratio of men to women is about three to one

No one constitutional type of individual is affected Most

cases are seen in physically well-developed persons Rarely is direct trauma a predisposing cause Benign growths such as papillomas of the bronchus may play a rôle, though these are rarely found postmortem

Etiology—As in other forms of carcinoma, we do not know the exciting agent of bronchial cancer Chronic irritation from smoke, dust, or chemical agents probably is the most important predisposing cause To this must be added chronic suppurations as in bronchiectases or cavities, tuberculosis, syphilis, foreign bodies, and possibly influenza

Street dust, coal dust, stone dust, tobacco smoke, and especially exhaust fumes from gasoline and oil of automobiles have been blamed We know the cancer-producing properties of certain coal-tar products, and perhaps it is these which cause chronic inflammatory changes with metaplasia of epithelium and cancer formation The writer has seen 8 of 40 cases observed in the past seven years, in foundry workers who handled acid fumes, garage employees, stone-cutters, and people employed in dusty occupations The increased use of gasolines, oils, and tar products may be an important factor in causing the increase in bronchial cancer in the last two decades Fibroid processes in the lungs (tuberculous and non-tuberculous) with the formation of bronchiectatic cavities produce a chronic bronchitis, lead to the accumulation of purulent secretions and foreign particles Epithelial thickenings, metaplasia, and leukoplakia form precancerous lesions Perhaps here as in other organs a hereditary predisposition is a factor

Pathology—Three types of primary carcinoma are possible in the lung (1) Carcinoma from the cylindrical bronchial epithelium, (2) carcinoma from the bronchial glands, (3) carcinoma from the alveolar epithelium We are concerned here only with the first type, the true bronchus carcinoma which constitutes about 90 per cent of all lung carcinomas

Histologically the bronchus carcinomas may be divided into (1) Squamous-celled (40 per cent), (2) basal-celled (30 per cent), (3) undifferentiated, more or less round-celled (30 per cent) The microscopic pathology does not concern us here

Bronchus carcinoma usually originates in a main bronchus, less often from a branch of the first to third order The right lung seems to be affected more often than the left, the ratio being about three to two The upper lobes are more often involved than the lower As we shall see later, the location is a very important factor in diagnosis, for the tumors of the lower lobes are much more difficult to recognize The small centrally located tumors may be found only on x ray examination The early hilum type may escape diagnosis for a long time unless x ray pictures are taken or metastases develop

Classification —The gross appearance of the tumor varies greatly, and also depends largely upon its location The cancer usually has a grayish or yellowish color Its size may vary from a small mass projecting into a bronchus or a small area of epithelial thickening to a tumor involving an entire lobe or lung For convenience in discussion of the pathology and clinical findings we may classify the bronchial cancers as follows

1 Endobronchial
2 Hilar
3 Mediastinal
4 Central
5 Lobar
6 Pleural
7 Rheumatoid

Characteristics of the Different Types —1 *Endobronchial* — In this form the tumor may remain symptomless for months Only direct bronchoscopic examination might reveal the small area of epithelial metaplasia and thickening, or the small area of cylindrical thickening and stenosis Or we may find a small papillary mass projecting into the lumen and partially or totally occluding it Bronchography may visualize a filling defect With obturation and atelectasis of the affected lung portion the diagnosis is easier Breath sounds are reduced or absent There is a darkening of the area, the diaphragm is elevated, and on inspiration the mediastinum may be drawn toward the affected side Metastases may occur even before there are any pulmonary symptoms It is important to know that in practically

all cases of bronchus carcinoma, large or small, there are metastases in the tracheobronchial lymph-nodes The significance of this fact will be discussed later

2 *Hilar*—This type is important because of its frequent occurrence, and the fact that it can be diagnosed in the early stage by x-ray examination In the early stage the physical findings are negative or indefinite A paravertebral area of dulness at the level of the fourth or fifth dorsal spine may be present The x-ray examination reveals an enlargement of the hilum shadow, with a network of fine branching stripes which radiate into the surrounding lung tissue Sometimes the larger bronchi, which normally are invisible, appear as double-contoured bands with lighter lumen The normal branching blood-vessel shadows of the hilum become fused together

In other cases more or less sharply outlined convex or lobulated hilum shadows appear They represent the enlarged infiltrated hilum lymph-nodes, and may be difficult to differentiate from enlarged glands in tuberculosis, lymphogranuloma, or lymphosarcoma In contrast to the enlarged gland shadows of tuberculosis we find the outline more irregular, with many dendritic projections into the surrounding lung tissue

From the carcinomatous hilum lymph-nodes, with their surrounding perivascular and peribronchial "lymphangitis carcinomatosa," the tumor may spread to involve an entire lobe or the whole lung The opposite hilum soon undergoes similar changes The pleura is reached Spreading through the pleural lymph-vessels, and along the bronchi and blood-vessels a characteristic x-ray picture is produced An interlacing network of fine spiderweb-like lines, with more dense spots where these lines intersect, produces the picture of a "lymphangitis carcinomatosa" To one who is not acquainted with such a film, the condition may be diagnosed as a miliary tuberculosis In this form the lymph-vessels of the lungs are filled with a cancer-cell network, due to retrograde extension from the hilum along the blood-vessels and bronchi to the pleura In the pleura the carcinoma spreads through the elaborate network of lymph-channels Minute nodules appear Later effusions may develop

3 *Mediastinal*—We have already mentioned the fact that the tracheobronchial lymph nodes are involved early in the disease Other mediastinal lymph nodes are also invaded The mediastinal masses may reach a tremendous size, and produce all the clinical symptoms of a mediastinal tumor, and yet the primary bronchus carcinoma remain very small The differentiation from a hyperplastic tuberculosis, lymphogranuloma, lymphosarcoma or aortic aneurysm may become very difficult The writer is reminded of a case which he saw in Vienna in 1925, which was diagnosed by internists and roentgenologists as a large aortic aneurysm The autopsy revealed a huge, almost spherical metastatic gland mass resting on the arch of the aorta The primary growth was a small bronchus carcinoma in the left lower lobe behind the heart In another case which was diagnosed as mediastinal Hodgkin's disease, the histologic examination of a supraclavicular gland showed a basal-celled carcinoma The postmortem revealed a small bronchus carcinoma in the right upper lobe.

Cough, marked dyspnea, hoarseness due to involvement of the recurrent laryngeal nerve, inequality of the pupils, cyanosis, and edema of the neck and face with venous engorgement are the usual symptoms There is of course the mediastinal dulness on percussion There may be a bronchus stenosis or paralysis of the diaphragm Part or all of one lung may become atelectatic or infiltrated

4 *Central*—In this type an early diagnosis is only possible with the *x* ray Like a central benign tumor, or echinococcus cyst, or pneumonia, there may be no physical findings on percussion or auscultation The *x*-ray reveals a central more or less homogeneous shadow in which lung markings are still distinguishable Unlike the benign tumor, or cyst or tumor metastasis, the shadow fades out into the surrounding lung tissue, and usually sends out tumor strands in all directions It may stop for some time at an interlobar fissure, or lead to an interlobar effusion or empyema Later the tumor shadow spreads to an entire lobe or lung field It reaches the pleura, producing a hemorrhagic effusion or lymphangitis carcinomatosa It may cause

the margin of the affected lobe to bulge into the adjacent lobe, in contrast to the retraction of the margin in tuberculosis or other fibroid processes At times central necrosis with infection leads to cavity formation with lung abscess or gangrene Tumor particles may be found in the sputum Undoubtedly some of the cases classified as lobar or pleural in type begin as central tumor masses, but are not seen at this early stage In the central form, as in all the others, metastases in the hilum glands and along the perivascular and peribronchial lymphatics occur With abscesses or bronchiectases, or even without these secondary changes, the writer has found clubbing of the fingers in most of these cases In 3 cases of this group there was a toxic hyperplastic periostitis Metastases may produce the first clinical symptoms Some of these centrally located carcinomas belong to the alveolar epithelial cancers The majority develop around a centrally involved bronchus of the second or third order Repeated x-ray photographs may be necessary to make a diagnosis The later photographs may show smaller tumor nodules around the periphery of the central shadow

5 *Lobar*—The lobar form of bronchial cancer is one of the most common types It is seen more often in the upper lobes than in the lower Whereas the diagnosis in the upper lobe is as a rule easy to make even in the early stage, it may be very difficult in the lower lobe without x-ray examination

The upper lobe bronchial cancer is characterized by a peculiar flatness of the median portion of the infraclavicular fossa on percussion In this early stage the patient may still have one to five years to live The area of flatness extends beyond the manubrium to its opposite border, in contrast to the dulness or flatness of a tuberculosis or pneumonia Over the area the breath sounds may be weak and the auscultatory findings minimal for such marked dulness With marked infiltration of the lung tissue there is bronchial or tubular breathing The entire lobe becomes consolidated The physical findings often closely resemble those of a chronic fibroid unilateral tuberculosis, or an unresolved pneumonia Unlike tuberculosis, the other lung and the apices are usually free from changes There is no denudation

of the heart as in tuberculosis The sputum, which in fibro ulcerative tuberculosis is positive, contains no tubercle bacilli, it is often blood tinged, and there may be fragments of tumor tissue There is usually severe pain, often referred to the shoul der Symptoms of venous stasis of the face, neck, and arm ap pear There may be hard enlarged supraclavicular or axillary lymph nodes

In the late stage various secondary changes may alter the clinical picture Often bronchiectases develop There may be bronchus stenosis with atelectasis as well as fibrosis Abscess or gangrene may follow On the affected side there is often a paresis or paralysis with high position of the diaphragm The chest wall is retracted, the respiratory movements are greatly reduced, the intercostal spaces become narrowed The heart, aorta, trachea, and esophagus are drawn toward the affected side as a rule The mediastinal structures become imbedded in the dense scirrhous tumor mass

When the tumor is on the right side the superior vena cava sooner or later is compressed The writer has seen invasion of the pericardium and myocardium in 3 cases In one case of bronchus carcinoma, of the left upper lobe, the patient developed the symptoms of a pulmonary stenosis, with a systolic murmur over the pulmonary area dilatation, and finally decompensation of the right heart The autopsy showed the pulmonary artery surrounded by the tumor mass, and so compressed that its lu men was reduced to a narrow slit

It should be stated that in any of the above five types of bronchial cancer a bronchopneumonia or lobar pneumonia may develop Such a pneumonia produces an enlarged tumor shadow which later disappears In several cases we have observed a lobar pneumonia which underwent delayed resolution In stead of a restitutio ad integrum a large hilum shadow or partial consolidation persists This later reveals its true identity Or the pneumonia associated with the bronchus carcinoma may lead to the empyema or lung abscess or gangrene

The *x* ray findings in the lobar form resemble those in lobar pneumonia or phthisis with the following exceptions

1 The infiltration is usually not limited by the interlobar fissure, but invades the adjacent lobe and has an unsharp outline Infiltrating strands can be seen at the tumor margin

2 The hilum shadows are usually enlarged Sometimes the lymph-node metastases are distinctly visible A finding which has been of greatest value to the writer has been the presence of a tongue-like projection downward from the hilum region on the affected side, sometimes on both sides This is absent in tuberculosis and pneumonia Furthermore, in fibroid tuberculosis of the upper lobe, the lower margin (fissure between upper and middle lobe on the right side) is usually drawn upward and is sharp In lobar bronchus carcinoma the margin is unsharp, with radiating strands running downward, and often projects downward into the middle lobe

3 Repeated x-ray films reveal an extension of the infiltration instead of a resolution

4 In bronchus carcinoma the mediastinum is usually drawn toward the affected side, with fixation The heart and aorta may be pulled upward as well The esophagus is often drawn toward the affected side

5 There is often a phrenic nerve paresis or paralysis, with a high position of the diaphragm and paradoxic movement

6 Iodized oil injections may show the bronchus stenosis or filling defect Bronchiectases frequently occur from compression

7 The intercostal spaces are often narrowed

8 When in the lower lobe, a large pleural exudate is usually present Aspiration may be necessary

9 A lymphangitis carcinomatosa, as already described, may be visible

6 *Pleural* —This type can develop as a later stage of any of the above forms, or may develop very early in the disease The pleura becomes involved either by expansion of the growth until it reaches a pleural surface, or more commonly by retrograde lymphatic extension from the hilum glands along the blood-vessels or bronchi In bronchus carcinoma of the lower lobe the pleurisy may entirely conceal the tumor mass The effusion is usually hemorrhagic It may cause a flatness of the entire

lung field, and the *x* ray examination reveals an intense darkening of the area. No structures are visible Aspiration of the fluid and injection of air help in making the diagnosis

In some cases a diffuse thickening of the pleura occurs with little or no hemorrhagic exudation, and the condition resembles the so-called pleural endothelioma (really a carcinoma)

In contrast to tuberculous and other large exudates the exudate in bronchial cancer, as a rule, does not displace the mediastinal structures (heart, trachea) toward the opposite side They are more likely to be drawn toward the affected side This is due to the marked fibrosis and scirrhus changes produced by the tumor The mediastum becomes immobilized The exudate should always be carefully examined for tumor cells Sometimes a small plug of tumor tissue is removable with a large needle or trocar and the diagnosis made possible

7 *Rheumatoid*—In this type of the disease rheumatoid pains in the extremities, spine, ribs, pelvis, or skull may be the first symptoms *x-Ray photographs may reveal metastases* These may be (1) osteoplastic, with increased density of the bones due to bone apposition or (2) osteoclastic, with bone destruction A negative *x* ray photograph does not yet rule out bone metastases There is another type—(3) indifferent, without any changes in the *x* ray picture These can be diagnosed only by microscopic examination

A second group of cases reveals no bone metastases but instead a hyperplastic periostitis This toxic periostitis is characterized by a peculiar irregular periosteal thickening on the diaphysis of the long bones (femur, humerus, tibia, fibula, radius, ulna, phalanges) The writer has seen three such cases The last case was seen in consultation about two years ago The patient had intense pain in the femurs A diagnosis of sciatica had been made All the teeth had been extracted, but the patient's condition grew worse A roentgenologist diagnosed a luetic periostitis, although the Wassermann test was negative From the *x* ray photographs of the legs the writer made the diagnosis of a toxic hyperplastic periostitis, due to a tumor of the lung The following day an examination of the patient re-

vealed a bronchus carcinoma in the right lower lobe The patient also had clubbed fingers

The blood examination, when there are bone-marrow metastases, may show a subleukemic myelosis We shall discuss this later

Metastases may occur anywhere in the body as with any malignant neoplasm There are, however, certain peculiarities which the writer has observed that may be of value in diagnosis That lymphogenic spread to the hilum glands practically always occurs has already been emphasized The retrograde lymphatic extension along the blood-vessels and bronchi leads to the characteristic x-ray findings The pleural involvement may result in (1) lymphangitis carcinomatosa, (2) extensive pleural effusion, (3) diffuse thickening of the pleura

Of the metastases to other parts those to the bones are among the most common These we have described under the rheumatoid type of the disease The true metastases may be (1) osteoplastic, (2) osteoclastic, or (3) indifferent Two or more types may be found in the same patient A pathologic fracture may be the first indication of a malignant growth The writer has seen one such case involving the femur It is important for the clinician and pathologist to realize that the primary bronchus carcinoma may be so minute as to be overlooked In a few cases pinhead-sized primary tumors have produced extensive metastases In every case of carcinoma metastases with an occult primary growth the whole bronchial tree should be searched very carefully

When bone metastases occur the writer has found them most frequent in the upper end of the femur and humerus Here they are usually osteoclastic They also occur in the ribs, spine, skull, etc In the spine a kyphosis resembling Pott's disease may result Or there may be a transverse myelitis due to pressure upon the cord

Next to the osseous metastases in frequency come those in the lungs themselves These assume the appearance of other pulmonary metastases They are usually multiple, round, sharply defined, and easily distinguishable from the primary growth

The liver is a frequent site for bronchus carcinoma metastases The liver may reach a tremendous size, and be riddled with small or large masses On the surface the nodules present the characteristic central depression or "cancer navel" due to necrosis and contraction This may occur in primary tumors of the liver as well

The writer has seen 4 cases with brain metastases It is, therefore, obvious that in people of middle age with brain tumor a metastatic bronchus carcinoma must be considered, and the chest carefully examined In one of our cases the autopsy revealed a brain abscess The periphery of the abscess contained carcinoma tissue The primary growth was in the lung

The kidneys and adrenals may become involved One case presented at autopsy metastases in both adrenals, but no complete destruction of the medulla or cortex There were no clinical symptoms of Addison's disease

Blood Findings.—In 3 cases the writer has found a leukemic blood picture, which might have been confused with a true myeloid leukemia It is an interesting fact that any carcinoma metastases in the bone marrow may cause a myeloid reaction with the discharge of abnormal cells into the blood stream The white blood count is in such cases 20,000 to 40,000, rarely above 75,000 The large number of myelocytes and normoblasts, associated with a secondary anemia, enables one to definitely diagnose bone-marrow metastases

The findings may resemble those in a true myelosis But the spleen is not enlarged nor is the liver, and the white count does not reach such high figures as 100,000 or more The anemia is of the secondary type with the color index below one

Extensive bone metastases may also be present without any blood changes Apparently the bone-marrow reacts differently in different individuals We have already stated that the metastases may be osteoplastic, osteoclastic, or indifferent They may or may not cause an erythroblastic or myeloblastic reaction The myeloid blood picture indicates metastases, its absence does not exclude them A similar reaction may be found in tuberculosis or lymphogranuloma of the bone marrow

Symptoms —From our discussion of the different types of bronchus carcinoma, we have already seen that the physical findings vary greatly with the size and location of the tumor, its type, the complications, location of metastases, and stage of the disease

In the early stage there may be no symptoms on physical examination The *x*-ray may reveal a suspicious hilum shadow, or central tumor, or early pneumonic infiltration There may be the general symptoms of an incipient tuberculosis, such as loss of weight, weakness, and subfebrile temperatures The onset may be very insidious with the development of a persistent unexplained cough The sputum may be blood-tinged at times Tubercle bacilli are not found on repeated examinations There is often pain in the chest, which becomes progressively more severe It may be an intercostal pain, or only limited to the affected area Often it is transmitted to the shoulder and arm As the pain increases it is hardly relieved even by opiates Pain in the osseous system may be due to metastases or periostitis Soon a dyspnea occurs with no cardiorenal cause In some cases the picture of a bronchial asthma appears, and the chest becomes emphysematous There is a violent, often paroxysmal cough This may be so severe as to produce epigastric pain and vomiting

The first finding may be an idiopathic pleurisy There is no previous history of pneumonia or tuberculosis If there is pain, it is not relieved by the effusion, nor does the dyspnea disappear after aspiration

Cough —When a patient over forty years old develops a persistent dry barking cough which does not react well to the usual therapy one should suspect a bronchus carcinoma A condition resembling bronchial asthma may occur It is not relieved by adrenalin or atropin A mucoid or bloody sputum appears With bronchiectases or abscess it becomes purulent Sometimes tumor tissue particles are expectorated

Dyspnea —Next to the cough the most important symptom is the marked dyspnea It is due largely to the pressure of enlarged tracheobronchial glands and tumor infiltration, fibrosis,

and narrowing of the trachea or bronchi, compression atelectasis of lung tissue Sometimes pressure upon the vena cava or pulmonary artery develops

Pain in the chest occurs early and is often the most important symptom. It is severe, out of all proportion to the physical findings It may be sharp and lancinating, or continuous It is increased by percussion It is often intercostal The pain may radiate to the shoulder or neck Severe headache suggests brain or skull metastases. Pain in other parts may be due to metastases

Cyanosis and edema of the face and neck are present in at least 50 per cent. of the cases They are due to the pressure of mediastinal masses on the superior vena cava or the large veins of the neck. Sometimes the pericardium is involved There are all the symptoms of mediastinal tumor

Hoarseness due to paralysis of the vocal cord on the affected side, sometimes on the opposite side, is a late symptom The recurrent laryngeal nerve becomes imbedded in tumor tissue

Fever is present in about one-third of the cases It is usually subfebrile, unless a pneumonia, lung abscess, or empyema develops.

Clubbed fingers, or watch glass finger nails, occur in about 10 per cent of cases Most of these are associated with bronchiectases or abscess The writer has seen 2 cases without abscess or demonstrable bronchiectases

Anisochoria.—Inequality of the pupils may result from pressure upon the sympathetic ganglia of the affected side The pupil on the affected side is usually smaller

Duration.—The length of life in bronchus carcinoma is quite variable and depends upon the location and malignancy of the tumor as well as upon the nature of the complications and site of the metastases. Death rarely occurs in less than three to six months. The average expectancy of life is about one year The writer has seen one patient who lived five years Pneumonia, lung abscess, or empyema may end the patient's suffering Death may be due to right heart failure

Therapy.—Unfortunately, we have no satisfactory treat-

ment for this disease A few cases have been reported as cured after lobectomy Only in very early cases with favorable location of the tumor is this advisable a-Ray treatment may relieve the pain temporarily, but the writer has seen no cures with deep therapy In most cases the growth of the tumor is unaffected The failure of the a-ray to influence the tumor growth may even be of diagnostic value

The treatment is only palliative The patient requires large doses of morphin or its derivatives for the relief of the intense pain Large effusions should be withdrawn Empyema requires drainage, if possible

CASE REPORTS

We shall cite briefly the last 4 cases of bronchial cancer, seen within the past year A complete summary of all our cases will appear later

Case I —The patient is a male aged fifty-six From 1890 to 1910 the patient worked as a coal miner From 1913 to 1927 he worked in a garage where he was constantly exposed to the exhaust fumes from automobiles

The patient's illness began one year ago when it was diagnosed as asthma by his family physician For the past six months he has had pain in the legs, especially the left thigh, and in the back The symptoms on entrance October 19, 1929 were marked dyspnea, a persistent cough with violent seizures of coughing followed by vomiting at times For the past month there has been considerable whitish-yellow expectoration A few times some blood was noticed The patient has severe pain in the left femur The patient's appetite is good For the past three weeks he has had frontal headaches The patient's temperature on entering was 98 4° F , the pulse 90 and regular, the respiration 28 The blood-pressure was 140 systolic and 94 diastolic.

During the stay in the hospital the temperature was never above 98 8° F The pulse varied between 72 and 96, the respiration between 18 and 40 Morphin was necessary to relieve the pain in the chest and legs An injection of adrenalin had no effect on the patient's asthmatic attacks

Of the physical findings we shall mention only those of direct interest. The patient is a well-developed man with an emphysematous chest and low position of the diaphragms Examination of the chest reveals numerous moist râles at the left base in the left phrenico-vertebral triangle The left diaphragm is fixed There is a triangular area of dulness which begins at the seventh dorsal spine and runs downward to the left diaphragm which is at the level of the eleventh spine The area is about 4 by 5 by 4 inches in size There is also a paravertebral area of dulness about 2½ by 1½ inches in size at the level of the fourth to sixth dorsal spine on both sides Over the triangular

area of dulness there is bronchial breathing There are a few rales at the right base. The findings caused the writer to suspect a bronchus carcinoma in the left lower lobe. This was confirmed by the x ray findings (Figs 183 184) A fluoroscopic examination also showed an osteoclastic metastasis in the left femur This was confirmed by the photograph

Fig 183.—*Case I* The x ray photograph reveals an area of infiltration in the left lower lobe, largely hidden by the heart This shadow fades out at the periphery Both hilum shadows are enlarged with the characteristic dendritic projections into the lung tissues A network of lymphangitis carcinomatosa is also visible

Bronchus carcinoma of the left lower lobe. Hilar involvement Lymphangitis carcinomatosa

Case II.—The patient is a male aged forty four For the past twenty four years the patient has been working at his trade of sheet metal worker He was constantly in the environment of acid fumes chiefly muriatic acid sal ammoniac, and other chemicals

The patient's ailments date back for a period of five years during which time he has had a cough. The last two years there has been more or less purulent expectoration. The patient himself noticed that the cough was more

severe after lying on the right side He was able to work until five months ago when he developed pain in the right chest This began beneath the right nipple and spread upward over the upper half of the right lung field A month later he developed pain in the left chest as well Soon the pain became more or less continuous and the patient got no relief During the past four months he lost about 30 pounds, and had frequent night-sweats with some fever in the mornings The patient then consulted his physician who sent him to a tuberculosis sanatorium in Colorado While there two new findings developed The sputum became blood tinged and has remained so for the past month Also about three weeks ago he quite suddenly became hoarse and has remained so Bacilli were never found

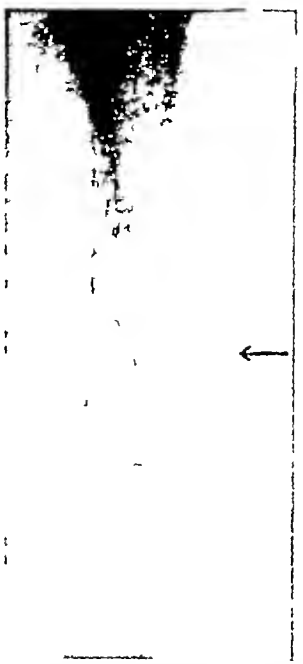

Fig 184.—*Case I* Photograph of the left femur revealing an osteoclastic metastasis There was severe pain in this region

On entrance to the Cook County Hospital on October 16th, the patient's temperature was 98° F , pulse 96, and respiration 22 The blood-pressure was 98 systolic and 58 diastolic. Physical examination shows a very well-developed man There is a slight asymmetry of the chest with retraction of the upper part of the right side On breathing the mobility of this part is reduced The trachea is drawn slightly to the right On percussion there is flatness over the upper right lung field down to the level of the fifth dorsal spine, and dulness down to the seventh There is a paravertebral dulness on the left side from the fourth to the sixth dorsal spine The area of flatness offers a peculiar resistance on percussion In front the flatness extends down to the level of

the fourth rib The whole area has bronchial breathing with numerous rhonci and some moist râles. There is a suggestion of amphoric breathing below the right clavicle There is some swelling of the neck with a group of hard, enlarged lymph nodes in the right supraclavicular fossa The veins in the right chest wall are distended The diagnosis of a lobar type of bronchus carcinoma in the right upper lobe was made, and confirmed on x ray examination (Fig 185)

Fig 185.—*Case II* The photograph reveals the typical picture of a lobar type of bronchus carcinoma in the right upper lobe There is abscess formation below the right clavicle Note the irregular lower border of the lobe and the tongue like downward projection of the enlarged hilum glands with radiating stripes into the lower lobe. There is also enlargement of the left hilum. The right diaphragm revealed a paresis The patient died three weeks after the photograph was made.

Case III.—The patient is a male aged sixty five For the past year the patient has had severe pain in the right chest In the last three months it has become so intense that the patient is unable to sleep at night unless he receives morphin The pain radiates into the right shoulder and down the right arm For the last month the patient has developed a bloody expec

toration The sputum is mostly mucus and not purulent Several times small quantities of pure blood were expectorated The patient had been treated for rheumatism of the right shoulder and neuritis In this case there was no history of exposure to chemicals The patient was a store keeper and had lived in the city all his life

The physical examination revealed findings almost identical with those in Case II The same flatness on percussion which extended across the manu-

Fig 186 —*Case III* Another typical x-ray picture of bronchus carcinoma of the right upper lobe Note the convexity of the lower border, with the tumor strands invading the middle and lower lobes The left hilum is enlarged and reveals large lymph-node shadows There is a beginning pleural effusion in the right phrenico costal angle There was a paresis of the right diaphragm

brium to the opposite border was present The entire upper half of the right lung was involved There was no Krönig field obtainable over the right apex There was bronchial breathing over the entire area with many moist râles Again a paravertebral dulness from the fourth to the sixth dorsal spine was found The right diaphragm was fixed There were enlarged glands in both supraclavicular fossæ and in the right axilla A diagnosis of bronchus carcinoma involving the entire upper lobe was made and confirmed by the *x*-ray

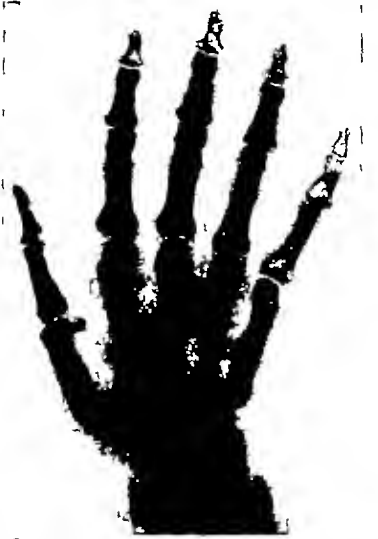

Fig 187.—*Case III* Right hand of same patient as Fig 186 Note the toxic hyperplastic periostitis of the metacarpals and phalanges. There was marked clubbing of the fingers

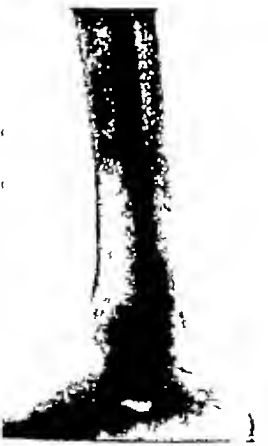

Fig 188.—*Case III* Left leg of same patient as Fig 186 Note the toxic hyperplastic periostitis of the tibia and especially the fibula.

photographs (Figs 186–188) The extremities presented a striking toxic hyperplastic periostitis of the tibia, fibula, metacarpals, and phalanges

Case IV —The patient is a male aged forty-five He was by occupation a peddler His first complaint was intense pain in both legs, especially the left thigh This became so severe that he consulted his family physician who made the diagnosis of a sciatica The physician ordered extraction of all the teeth The pain, however, continued to get worse An x-ray photo graph of the left femur was ordered by the physician The roentgenologist reported a syphilitic periostitis The Wassermann test was negative The

Fig 189 —*Case IV* Central type of bronchus carcinoma in the right lower lobe Note the unsharp and irregular outline of the shadow, also the adhesion to the right diaphragm Both hilum shadows are enlarged

writer was called in consultation on the x ray photograph He suspected a toxic hyperplastic periostitis, most likely due to a tumor of the lung, and predicted that the patient might also have clubbed fingers An examination of the patient the following day revealed definite clubbed fingers There was a circular area of dulness about 4 inches in diameter just above the right diaphragm posteriorly The right diaphragm was fixed *x*-Ray examination revealed a central type of bronchus carcinoma in the right lower lobe (Figs 189, 190)

Fig 190.—*Case IV* Left femur with the toxic hyperplastic periostitis Note the periosteal thickening on the diaphysis as well as sclerosis suggesting osteoplastic changes.

SUMMARY

Bronchus carcinoma is not a rare disease It constitutes today about 7 per cent of all malignant tumors The disease is more common in men than women It usually occurs between the ages of forty and sixty

A persistent cough, expectoration of blood tinged sputum, pain in the chest, or attacks of asthma are the usual early symptoms In some cases, a subfebrile temperature, weakness, and some loss of weight may cause the physician to suspect tuberculosis A hemorrhagic pleural effusion in an otherwise healthy middle-aged patient should arouse suspicion The violent cough ing, intense pain, cyanosis, and marked dyspnea are later symptoms

To emphasize the great variability of the clinical and patho-

logic findings the writer has classified the bronchial cancers into (1) endobronchial, (2) hilar, (3) mediastinal, (4) central, (5) lobar, (6) pleural, and (7) rheumatoid, and described the characteristics of each type

The Roentgen ray is an indispensable aid in the diagnosis of the primary growth as well as of the metastases Often repeated examinations are necessary before a definite diagnosis can be made

A myeloid blood-picture, or toxic hyperplastic periostitis, or metastases in the osseous system should be sought in all cases The lungs, liver, bones, and brain are frequent sites for metastases

The disease is unfortunately incurable Most patients die within two years Some few live four to five years

CLINIC OF DR SIDNEY A PORTIS

LOYOLA UNIVERSITY MEDICAL SCHOOL

THE RELATION OF HEADACHE TO UPPER ABDOMINAL DISTRESS

I AM going to present this morning three histories of patients complaining of upper abdominal distress, associated with headaches and nausea, and in one case, vomiting These histories are of particular interest because they emphasize the rôle of the upper intestinal tract in producing the above symptomatology The discussion will be given later

Case I.—The first patient is a young unmarried girl E. L aged twenty four born in Illinois whose occupation is that of a stenographer Her main complaint was headache She stated that for some time she had been troubled with headaches which had been rather generalized but more pronounced in the occipital region Her vision had been tested glasses given for the refractive error and very little improvement had been noted For the last five months in spite of the correction of her refractive error the headaches had been more or less constant They were occasionally sharp but for the most part were a dull ache She had had no spots before the eyes no notable twitchings, vertigo tinnitus or stuffiness in the ears She had had some nausea but no vomiting or belching She had had no cough night sweats nor loss of weight Her bowels were regular and moved one or more times daily Her appetite had been good. She had to urinate occasionally frequently during the day but there was no nocturia dysuria or burning

Her family history was essentially negative There was no history of headaches tuberculosis or carcinoma Other than childhood diseases her past history was of no noteworthy importance and there had been no surgical manifestations. Her menstrual history was essentially negative of the usual duration and flow and the headaches were not aggravated at the menstrual period. She was active slept well and indulged in coffee and tea moderately but not in alcohol or tobacco

Physical examination revealed a fairly well-developed female weighing 100½ pounds with a blood-pressure of 100 systolic and 70 diastolic, temperature and pulse normal. The eyes were essentially negative. There was a fine

tremor of the hands and tongue, and the reflexes were normally intact The tonsils showed quite an enlargement with small regional adenopathy The thyroid gland was slightly enlarged, the lungs were normal, as was the heart She was distinctly tender in the region of the appendix. Her spleen was not palpable, and the rest of the abdomen was negative Other than the regional cervical adenopathy there were no demonstrable glands superficially elsewhere Rectal examination revealed the uterus to be somewhat retroverted, with some tenderness posterior to the uterus, however, no distinct masses could be felt and there was no evidence suggestive of inflammation in the appendages The urine was essentially negative The stool contained no occult blood and there was a slight increase of undigested fat, starch, and muscle-fiber The bacterial flora resembled the usual horm The stomach acids were 30 free, and 40 total on a motor meal, with no evidence of retention and similar findings on an Ewald meal The hemoglobin was 86, red count 4,490,000, white count 9100 with a normal differential The Wassermann test was negative The blood chemistry was essentially negative except that the carbon dioxid combining power was 61 2 The basal metabolism was —9 The dental x-rays revealed a suspicious left lower molar

The x-ray of the chest and abdomen revealed that the chest was essentially negative The stomach was 3 inches below the intercostal line, the duodenal bulb filled out normally There was surging in the second portion of the duodenum and the second portion encircled itself behind the bulb, and was seen high above the lesser curvature of the stomach There was definite stasis here However, the stomach emptied at the end of four hours Subsequent observations revealed a freely movable appendix, fairly well filled, which was distinctly tender x-Rays of the cervical vertebræ revealed no evidence of arthritis

Protein sensitization tests revealed numerous foods with a moderate allergic reaction The patient was put on a diet based upon these allergic reactions, with no improvement She was then given a suitable corset and pad and during the whole time that this was worn the patient showed almost complete disappearance of the headaches, and neglect to wear it caused a recurrence of the headache and subsequent symptoms Medication was purely symptomatic and seemed to have no effect on the headache syndrome until the above measures were used

Case II —M H , unmarried female, aged twenty-four, born in Russia, whose occupation is that of stenographer, complained of epigastric distress, which, previous to the consultation, had been present for some time. It was a dull ache coming on at any time, not related to or relieved by food, more or less constant There was no nocturnal distress There was some nausea and headache, but no belching or vomiting She perspired freely, but there had been no palpitation or hyperexcitability The distress was somewhat aggravated by bowel movement, and she had lost a few pounds within the last few months There was a slight tendency to constipation Her appetite was good There was no nocturia or dysuria, and the inventory of her systems other than above was essentially negative Her family history was essentially negative, as was the menstrual history The medical and surgical

history, other than influenza in 1918 had no bearing on her present complaint Her habits were within ' normal limits

Physical examination revealed o fairly well-developed female weighing 111½ pounds with normal temperature respiration and pulse The eyes were negative. The mouth and throat showed no evidence of gross pathology There was o slight enlargement of the thyroid The lungs were negative as was the heart. However the blood pressure measured 130 systolic and 80 diastolic. She was distinctly tender in the region of the oppendix and sig moid but there was no other demonstrable tenderness Reflexes were markedly exaggerated and there was n coarse tremor of the hands and tongue

The urine showed o very faint trace of olbumen nnd a slight increase of indican but otherwise was essentially negative The stool examination re vealed no occult blood but o slight increase in undigested starch ond a large predominance of Gram oegative flora.

The blood-count showed 83 per cent. hemoglobin 4 410 000 red cells 8/00 white cells with o normal differential The stomach neids on Ewald and motor meal were within normal llmits The Wassermann test was nega tive Ifer blood chemistry was negative except that the carboo dioxid com bining power was 59 8 The basal metabolism was +4 per ceot

Pelvic findings Rectal examinotion showed that the uterus was retro-verted definitely enlarged There was some tenderness of the left fornix and a small irregular swelling in this region There were some hemorrhoidal tags.

The fluoroscopic x ray revealed that the chest was essentially negative The stomach showed evidence of hyperperistolsis but no lesion was seen There was an occasional small spasm of the greater curvature side of the du odenal bulb. However it yielded to manipulation The secood portion of the duodenum took a course directly upward and showed cvidence of dilato tion and stasis The stomach was prolapsed 1½ inches into the pelvis. The stomach emptied ot the end of four hours. Subsequent observations revealed the bowel moderately spastic, filled throughout and n slight tenderness over an irregularly filled retrocecal appendix. Re-check of the stomach under the influence of belladonna revealed a complete disappearaoce of the hyperperis-talsis and a normally filled duodenal bulb However the stasis in the second portion of the duodenum was more marked The dental x rays revealed nu merous infected teeth.

The patient was put on a suitable low protein diet given symptomatic medicatson and a corset and pad but her symptoms continued for a period of four months Re-check of the x ray findings revealed sumilar evidence and surgical consultation was suggested She was seen by Dr H M Richter who advised an exploratory operation which was subsequently performed

The findings were that of a moderately thickened appendix with ooe small adhesion An appendectomy was done. There was also a very defi nitely dilated second and third portion of the duodenum whose course was directed upward and median to the duodenal bulb The finger could not be inserted beneath the vessels and ligament of Treitz. However there was no complete occlusion here. An anastomosis between the third portion of the

duodenum and jejunum was made The patient made an uneventful recovery from the operation Since this operation her upper abdominal distress has completely disappeared She has no nausea, no headaches, and has gained over 10 pounds in weight

Case III —The third patient, N G, white, unmarried female, aged forty-seven, complained of headaches and bloating of the abdomen, constipation, and "bilious" attacks Since the age of eighteen the patient had experienced recurrent frontal headaches on either side, over the eyes, coming on about once a week, occurring in the morning, and lasting a day or even two For the past three years she had experienced attacks of so called "biliousness" once a week, characterized by a bitter taste in the mouth, nausea and vomiting, and sometimes had vomited as many as five times during the night Vomitus was green and bitter and this symptom complex was usually associated with the headaches There had been no excess belching, no noticeable icterus, she had some bloating and gas pains occasionally two hours after meals, which lasted two or three hours, especially at night She had been constipated as long as she could remember, and took cathartics daily—cascara for the past six months There was no vertigo, tinnitus, cough, expectoration, hemoptysis, or edema The hands stiffened during the attack of headache She was very nervous, worried a great deal, and had lost 22 pounds in two years Her appetite was good when not ill She urinated twice each night, there was no definite dysuria

Past History—Her father died of apoplexy Her mother had organic heart disturbance One brother died of diphtheria, and three sisters were living and well There was no other constitutional or familial disease There was no history of other members of the family having similar attacks

Her menstrual history began at fourteen, regular, with dysmenorrhea, and she had an unexplained menopause at the age of thirty-seven She had the usual childhood diseases, diphtheria at twenty, pneumonia at twenty, and she had an attack of influenza at thirty-six Her appendix had been removed at forty-five, and she had had a hemorrhoidectomy a few years previous

She had insomnia, consumed 4 cups of tea daily, but otherwise her habits were essentially negative

Physical examination revealed a somewhat emaciated white female, about forty-seven years of age, with a normal temperature and pulse, and a blood-pressure of 122 systolic and 66 diastolic, who weighed 89¾ pounds The eyes reacted to light and accommodation with a slight extrinsic muscle weakness The tonsils were somewhat enlarged, not grossly pathologic. The teeth had been long since removed There was a fine tremor of the hands and tongue, and the reflexes were somewhat exaggerated The thyroid was firm, slightly irregular, but not materially enlarged The right apex was dull, but there was no evidence of activity noted The rest of the lungs were essentially negative The heart showed no definite murmur However, the tones were "snappy," and there was no demonstrable enlargement There was marked tenderness in the region of the epigastrium, less over the gall-bladder region There was an appendectomy scar and slight tenderness over the sigmoid The uterus was not enlarged, but was rather hard, there were no tumor

masses in the region of the adnexa Rectal examination revealed rather large internal hemorrhoids and external tags.

The urine showed a slight trace of albumen no sugar an occasional hyaline cast but was otherwise negative The stool contained a large amount of mucus some pus cells, no occult blood and a moderate amount of undigested starch and fats. The stomach acids were 15 free and 25 total on a motor meal with evidence of slight retention of raisin seeds but no sarcinæ were found The Ewald meal revealed 35 free and 50 total and both specimens contained no occult blood The hemoglobin was 78 red cells 4 500 000 and white cells 7800 with a normal differential The Wassermann test was negative The basal metabolic rate was plus 10 Her blood chemistry was within normal limits except for a slightly increased carbon dioxid combining power

Fluoroscopic x-ray examination of the chest and abdomen revealed that the right apex did not light up as well as the left There were small adhesions between both lungs and respective leaves of the diaphragm. The right complementary space was partially closed Heart and aorta were within normal limits. The stomach was markedly prolapsed into the pelvis, but showed no abnormal findings The duodenal bulb filled out normally but just below the bulb there was a large dilated pouch which gradually filled and remained filled It seemed to superimpose itself on the duodenum However the two could be partially separated The barium remained in this pouch for a long time. However when the patient was in the horizontal position on her back the pouch partially emptied itself At the end of four and one-half hours there was still some barium in what seemed to be the duodenal pouch Plates at five and one half and six hours showed similar findings The cecum at subsequent twenty four hour observation was held fixed in the brim of the pelvis and the rest of the colon was markedly prolapsed into the pelvis The radiographic evidence substantiated the fluoroscopic observations in giving similar findings.

This patient was operated on by Dr Bernard Portis under local anesthesia. On opening the abdomen it was noted that there were extensive adhesions in the right upper quadrant obliterating this space. On further dissection it was noted that there was a very large duodenal pouch like structure about 1 cm. beyond the pyloric ring This corresponded with the x ray findings. Subtotal gastrectomy was deemed advisable and performed in the usual manner On dissection of the stomach a small nodule was found in the pyloric ring resembling a small fibroma and subsequent histologic examination substantiated this opinion

The patient has gained over 20 pounds in weight during the last year has been free from headaches nausea and vomiting loses no time at her occupation and is perfectly comfortable Postoperatively she was put on ambulatory ulcer management with powders after meals and a tonic capsule between meals. She at this time is eating everything with no distress and no medication

DISCUSSION

I am particularly interested in presenting these 3 cases, not only because of their clinical and pathologic interest, but be-

cause of the economic importance of restoring these individuals to their normal mode of life and giving them the health to earn their daily wage

In the first case simple, conservative, and palliative management was all that was necessary, and many patients of this type respond to this form of management It is particularly noteworthy that they do better at first on a low protein diet which produces an aciduric flora in the colon and they have less of the so-called resultant intestinal toxemia It is interesting to note that in the palliative form of treatment the patients do not do well with the ordinary alkali, that with their partial duodenal ileus they have a potential alkalosis and that the distress is aggravated by the administration of alkalies When any neutralizing salt is needed, I prefer to use the tertiary phosphates of calcium and magnesium These patients require, in the palliative form, very little medication for their headaches per se because they have long since become used to these various remedies In addition, they should be encouraged, they should be made hopeful for the future, and given a much brighter outlook on life Enough laxatives should be used in a mild form along with suitable diets to keep the bowels moving regularly In addition, large amounts of acidophilous bacteria either in the form of milk, culture, agar cubes, or cheese, seem to be particularly valuable in this type of case Occasionally they are distinctly benefited by a diet based upon protein sensitization tests, but in one of these cases cited the tests were of very little help and only when this partial duodenal ileus was relieved by the aid of a corset and pad did the patient make a distinct clinical improvement

In the second case with a more definite roentgenologic evidence of duodenal stasis, but no ptosis as a factor in the production of it, it was thought wise, after medical management had failed, to have surgical intervention The result of the anastomosis of the duodenum with the jejunum not only relieved her headaches and her distress but also markedly benefited her associated duodenitis which at times presented a clinical picture resembling peptic ulcer Her postoperative diet was that

of an ambulatory ulcer patient Most of these patients do better postoperatively on this régime than if they select their diet haphazardly Finally, in the last case after the diagnosis was correctly made, medical management was refused the individual, and she was told that surgery was the only procedure in my judgment which would give her relief The wisdom of that course has proved itself by the clinical result obtained in this case

CLINIC OF DR CLARK W FINNERUD

CHILDREN'S MEMORIAL HOSPITAL

DERMATOLOGIC AFFECTIONS IN CHILDREN

GRANULOMA PYOGENICUM

THIS child age six years has a pea sized red soft pedunculated lesion of the left cheek near the jaw angle of between two and three weeks duration It is smooth and devoid of subjective symptoms The mother states that she believes a pimple of some sort was present here for a day or two when the child picked it. The small crust soon fell off but the red swelling has gradually and steadily increased in size

Granuloma pyogenicum affects with predilection the face and hands, but may occur on any area Usually there is but one lesion present The cause of this condition has not been proved, but it is thought to be produced by the pus cocci It occurs at all ages and about equally in the sexes The lesions occur most commonly at the site of an injury or in an area of skin which is the site of some sort of cutaneous eruption, this site having become infected with the causative organisms Not uncommonly, however, there is no history of preceding skin disease or trauma, the lesion making its appearance on what apparently was grossly normal skin The lesions range from the diameter of an ordinary match head to that of a hazel nut, and vary from bluish red to bright red Although the surface of such a lesion is usually smooth, it may be necrotic or crusted The lesions characteristically are highly vascular and bleed easily and profusely Generally speaking, they are rapidly growing They may be either pedunculated or sessile

It is a benign connective tissue new growth which histologically shows granulation tissue containing variable proportions

of young connective tissue and newly formed blood-vessels The cellular constituents of the lesions include polymorphonuclear leukocytes, lymphocytes, and plasma and mast cells

Granuloma pyogenicum need be differentiated chiefly from true angiomata, which ordinarily are slow-growing tumors In case of doubt a histologic examination may be resorted to by way of settling the diagnosis

A most satisfactory way of eradicating these lesions is by freezing with carbon dioxid snow, this procedure to be followed by the application of two or three skin units of Roentgen rays sharply limited to the lesion In case the lesion has not entirely disappeared within three weeks, this or a somewhat milder similar treatment may be employed Of course, radium may be used in place of x-rays The lesion may also be eradicated by excision, or by some form of cauterization other than that mentioned

Recurrence is not the rule, but in an occasional instance it is seen, and further similar treatment is, therefore, necessary

LYMPHANGIOMA CIRCUMSCRIPTUM

A child, age five years, has a disorder of the mucous membrane of the hard and soft palate in an area about the size of a silver quarter, which the mother states was first noticed by the family physician about five months previously, while examining the child's throat at the time of an acute bronchial infection The child had never been noticed to be in any way aware of the disorder

Examination shows a mottling of pinkish-yellow and dark bluish, millet-seed sized and larger, rather sharply circumscribed elevations thickly studding this area, lesions which have the appearance of minute, superficial and deep vesicles No similar lesions are present on the mucous membrane of the mouth elsewhere or of the pharynx or any place on the skin.

Lymphangioma circumscriptum is really the only form of lymphangioma which falls within the domain of the dermatologist The true cause of the disorder is unknown, it probably belonging to the nevi The disorder may be present at birth, but usually begins some time during early childhood

The lesions consist of one or more coin-sized groups of pinhead to match-head sized, minute cysts, which have the appearance

of deep-seated but well-elevated vesicles The appearance of such a lesion has been well likened to the appearance of frog's spawn The patch usually but one in number, occurs as a localized group of irregular shape, the surrounding skin, or mucous membrane and often that in between individual cysts, being of normal appearance The favorite sites of the disorder are the tongue pharynx, hard and soft palate, tonsillar areas, including the pillars, the lining of the cheeks, and the axilla and upper extremities The skin patches sometimes become of somewhat warty appearance The true nature of such a lesion may be ascertained by puncture in any areas of suspected involvement, in that usually upon puncture a clear rather glairy thick or watery fluid is exuded, a fluid which sometimes is tinged with blood

Histologically, one sees these lesions which resemble vesicles to be cysts which, for the most part, are located in the upper corium These lesions have an endothelial lining and sometimes are associated with dilatation and new growth of the blood vessels of the vicinity, and with either hypertrophy or atrophy of the constituents of the corium and epidermis There is enough blood content in some sections to warrant a more proper diagnosis of hemolymphangioma

Such a lesion, after progressing to a certain stage, rarely exceeding the diameter of a large coin, becomes stationary There is little or no tendency toward spontaneous involution

The lesions are best eradicated by destructive measures, radium, properly employed, being the agent of choice Here again, Roentgen therapy may be substituted for radium therapy, with or without the employment of carbon dioxid snow or other cautery

KERATODERMA PALMARIS ET PLANTARIS (HEREDITARIA)

This child age three years was brought in because of this thickening of the palms and soles which has been present since shortly after birth There are no subjective symptoms which the mother has been able to notice except when fissures form, at which time it is evident that the child experiences some discomfort. The mother has used several proprietary preparations as suggested by druggists, but has never seen a physician concerning this condition The child in every other respect is apparently healthy Two of five older brothers and sisters have this disorder in some degree none so markedly as

this child It is the mother's impression that one of her sisters and her mother have the same disorder in a milder degree

Keratoderma palmaris et plantaris may be either congenital or acquired The congenital cases are frequently with a history of the disorder having been present in more than one generation The acquired cases may begin at any age and are more commonly associated with hyperidrosis of the palms and soles, which gives the thickened skin somewhat of a "sodden" appearance Acquired cases may be occupational in origin, may be due to long-continued taking of arsenic, or may develop secondarily to some other dermatosis of this area, such as mycotic infection, psoriasis, or syphilis

The lesions consist of diffuse, hard, dry thickening of the skin of the palms and the soles, often actually transforming these areas into smooth, yellowish, translucent horny plates, or, this thickening may become of warty appearance and rather dirty looking, this last feature being seen more commonly in the congenital cases In rare instances, and chiefly in the acquired cases, the eruption consists of puncta and small plaques disseminated over these areas The involvement usually stops abruptly at the sides of the palms, soles, fingers, and toes, except in the vicinity of the joints, in which areas the same changes may be seen on the dorsal surfaces Hyperidrosis may or may not be associated In that the skin in these areas has become markedly thickened, upon movement it cannot bend and it therefore breaks Consequently fissures, often deep and painful, form

Histologically, one notes that there is marked hyperkeratosis, but that this cornification process, though excessive, is normal in type All of the epidermal coats may be thickened The corium usually is practically of normal appearance

Because of the absence of subjective symptoms, one is not likely to confuse this disorder with eczema or other itching dermatoses which might affect such areas Syphilis of the palms and soles, unlike keratoderma palmaris et plantaris, is usually an asymmetric disorder, in that such a manifestation of syphilis would need be a tertiary one In the acquired cases of kera-

toderma it is important that one ascertain the cause of the disorder, if possible, in that upon this treatment depends As stated, the cause of the congenital cases is unknown

Treatment.—In the cases of the type illustrated by this child all that can be hoped for is that the parts may be kept usable This can be accomplished by the prolonged use of keratolytic ointments and lotions, in that such preparations will dissolve the horny layer of the skin and thereby keep the parts pliable So far as general measures are concerned, care of the general health is considered of some importance, and, in adults, supposedly limitation of stimulants, such as coffee, alcohol, and tobacco, is advisable It is probable that intravenous injections of sodium thiosulphate would be of service in the cases which result from the ingestion of arsenic. If a fungus can be demonstrated to be causative in an acquired case, the usual treatment of such infection should entirely eradicate the disorder If psoriasis is causative, as evidenced by the presence of it on other parts of the body, treatment of that disorder should prove effective The same can be said of eczema If the disorder can be demonstrated to be of luetic origin, specific treatment for that disease is indicated and is effective Generally speaking, only the acquired cases can ever be entirely remedied, and even these are often extremely resistant to treatment.

LICHEN URTICATUS

This child age four years has a severely itching disorder of the trunk and extremities of two and a half months duration The mother states that the itching is so severe that it keeps the child awake n large part of the night and that there seems to be little or no irritation during the day She states that by looking at the eruption at present we can have no conception of the way that it appears at night in that during the night she notices numerous places which resemble mosquito bites and that these are not now present. The child has an older brother and sister and a younger brother none of whom is affected The mother further states that she is able to relieve the child somewhat by bathing the parts with a solution of soda. So far as she knows, the child is in every other respect perfectly normal. She has always followed the instructions of the Infant Welfare as regards the diet of her children.

Lichen urticatus is a form of urticaria which is peculiar to

infants and children, and which ordinarily disappears spontaneously at the age of puberty Its cause is unknown These cases seem to be more numerous and more severe during the warmer months The lesions occur chiefly on the trunk and extremities, evidence of the disorder for some reason very rarely being observed on the exposed portions of the body For the most part the lesions make their appearance during the night They consist primarily of match-head to pea-sized wheals, not unlike a mosquito-bite in appearance, in the center of each of which a minute papule or vesicopapule forms Because of the severe itching the child scratches this new lesion, thus excoriating the papulovesicle, and a small crust forms at the site The urticarial lesion disappears within an hour or two, so that all that remains at the site is a papular excoriation Therefore, when the patient is examined during the day, one simply sees blood-crusted, papular excoriations disseminated over the trunk and extremities, although there may still exist around some of these lesions a pinkish areola representing the site of the former wheal Not uncommonly, marked dermographism can be demonstrated by drawing the finger nail or an applicator across the skin in any place

Lichen urticatus must be differentiated chiefly from scabies In scabies there usually is a history of other members of the family being similarly affected, and there are characteristic lesions in that disorder from which the organism and its ova can be readily and practically invariably demonstrated It has been said that prurigo sometimes need be demonstrated from lichen urticatus, but the similarity is rather far fetched, prurigo being more like papular eczema Prurigo, though seen rather commonly in Austria and other European countries, is an extremely rare cutaneous disorder in this country

The treatment of lichen urticatus is far from satisfactory, but these patients can be given considerable relief during their attacks and can be assured that they will recover from the disorder eventually Internally, sodium bicarbonate in 3 to 10 grain doses in syrup of rhubarb, given after meals, is probably most often of service Locally, antipruritic lotions and ointments

are indicated, one of the most serviceable of which is a lotion composed of black wash and olive oil, to which has been added 15 c.c. of liquor carbonis detergens to the 8-ounce mixture, this to be applied as necessary for irritation

SCABIES

This group of three children a boy aged four years and two girls aged six and seven years have an itching disorder of the trunk and extremities of about a month's duration The mother states that she thinks she and her husband have the same thing but that the eleven months old infant is unaffected She states that the itching is worse upon retiring and that she believes her husband was the first one affected

Scabies is caused by an animal parasite, the *Acarus scabiei* which burrows in the topmost layer of the skin The organism is of much the same appearance as a louse, but much smaller being scarcely visible to the naked eye

Almost invariably the itching is worse at night, after the body has become warm in bed Considerable itching is often experienced during the day, however, when the body has become warm from exertion, from exposure to an overheated room, or from the wearing of excessive clothing Usually there are hundreds of thousands of the parasites present before the afflicted individual is well aware of the fact that he has a skin disease If one member of a family is affected, usually several or all of them are Most commonly the disorder is contracted through occupying a bed with an infected individual. The sites of predilection are the trunk and extremities, there being no sign of it above the collar bone or below the ankles, except in infants The most typical lesions are seen between the fingers and on the wrists, and here they exist as about match head sized vesicopapules, on the surface of some of which are seen a delicate, black, thread like, straight or curved line which varies from an eighth to a quarter of an inch or more in length. These lines are the visible paths of the parasite in the skin and consist of a furrow filled with dirt, eggs, and excrement of the organism Usually there are a dozen or more eggs in each furrow, and at one end of it is the parasite The eggs

give rise to new parasites which crawl out onto the surface of the skin Here the females, which are the only ones that burrow, are fertilized, the males remaining on the surface The female perishes after burrowing and laying her eggs On regions other than the hands, wrists, genitals, and buttocks the lesions exist chiefly as papular excoriations about the size of a pin's head, lesions which can hardly be recognized as those of scabies, at least without microscopic examination

In every case of suspected scabies the organisms or the ova should be demonstrated under the microscope, by way of clinching the diagnosis, this even in the presence of rather definite clinical history and findings This is done by slicing off the top of a lesion, putting it on a glass slide, applying a cover-glass, and allowing 2 or 3 drops of 10 to 20 per cent sodium or potassium hydroxid to run under the cover-glass After gently heating such a preparation, microscopic examination will reveal a parasite or its ova, or both, in case one is dealing with scabies

Probably the best treatment is the old-fashioned sulphur treatment which consists of applying a sulphur salve for five sucessive nights After taking a scrub-bath the infected individual should apply the salve from the neck to the ankles, including the hands A suit of underwear with long sleeves and legs should be worn continuously night and day, it becoming permeated with the sulphur, and thin cotton gloves should be worn at night On the morning following the fifth application of the salve a cleansing bath is taken and clean clothing put on Some itching may persist, but it is due to irritation of the skin by the sulphur This ordinarily is allayed by a few daily applications of olive oil For infants and young children a 5 to 7 per cent sulphur ointment is used, for middle-aged children a 10 per cent ointment is employed, and for adults one of 15 per cent strength The sulphur should be put up in plain petrolatum to which about 20 to 25 per cent of lard has been added Another sulphur preparation, one of rather complicated formula, known as the Danish ointment, constitutes a fairly satisfactory remedy for this disease, its greatest advantage being the fact that supposedly but a single application of it is necessary Having seen

many recurrences of the disorder from a single application of it, however, it has been found advisable to use it for two successive nights, by which procedure it is effective, though more irritating to the skin than is the former preparation

SCROFULODERMA

This Italian girl age nine years has three hazel nut sized swellings of the right side of the neck of about one year's duration and two ulcers here which have appeared within the last six or eight weeks There is no history of afternoon elevation of body temperature night sweats weakness or other general symptoms of interest There are two brothers and two sisters all younger and all well. There is no family history of tuberculosis although even with the aid of an interpreter history taking is rather unsatisfactory

Scrofuloderma consists of a direct extension to the skin of a tuberculous process from underlying structures of tuberculous nature, and, therefore, is seen chiefly in the vicinity of superficial lymph glands and over joints Probably nine-tenths of the cases exhibit lesions only in the cervical region of one or both sides The disorder usually begins in childhood and may never develop to the point of breaking down into ulcerations, such as are here present, but usually after lesions have existed as firm to doughy swellings for a period of six months to two or three years, there develop one or more such ulcers Infected glands are at first small and firm, about pea sized when first noted, and movable These gradually enlarge, sometimes even attaining the size of a hen's egg, and upon enlarging become adherent to the overlying reddened integument After becoming doughy to touch they later actually fluctuate, finally breaking down to form oval or linear ulcers with soft, undermined, reddish margins and a rather necrotic floor A seropurulent discharge may be present, or the lesions may be crusted Fistulæ not uncommonly connect two or more such ulcers Seldom are more than a half dozen lesions present, and these are usually localized to one side of the neck Ordinarily, subjective symptoms are present only before the lesion has completely broken down, and constitutional symptoms are variable Healing occurs with scarring which may be either atrophic or hypertrophic, and which often is quite disfiguring, regardless of the type of treatment employed

There is little likelihood of confusing a classical case, such as this one before you, with anything, although in some instances scrofuloderma must be differentiated from syphilitic gummata and more rarely from actinomycosis These latter disorders are seen usually in adults, whereas tuberculosis of the type described is one essentially of childhood In syphilis, other findings are to be expected, and in actinomycosis the ray fungus is demonstrable in fresh preparations and in cultures with but little difficulty In any instance, a histologic section or a therapeutic test should settle the diagnosis

Scrofuloderma is best treated by weekly small doses of neoarsphenamin given intravenously, along with well-filtered Roentgen rays over the involved area, these procedures combined with general measures which would tend toward building up the general body resistance of the individual, such measures being plenty of sleep, fresh air, nourishing food, sunshine, and tonics Surgical procedures need be resorted to in but rather a small proportion of the cases

RINGWORM OF THE SCALP

A boy, aged three years, and two sisters, aged five and seven years respectively, American born Polish children, come in because of loss of the scalp hair in patches The mother states that the other child, a nine-year-old boy, is not affected Apparently there are no subjective symptoms

Upon examination we see from three to a dozen finger-nail to large coin-sized patches of almost complete alopecia in these scalps The surface of each patch is grayish, finely scaling, and stippled with numerous hair stumps These stumps average from 1 to 4 millimeters in length, some of which are surrounded by a whitish sheath, and may be pulled out with the ease that a pin is removable from a pin-cushion Upon removal of the scales little or no gross sign of inflammation is seen in the underlying scalp

Ringworm is a disease of the skin, hair, and nails which is produced by numerous varieties of parasites belonging to the large group of fungi In children, ringworm is seen chiefly in the scalp, and practically all the cases of ringworm of the scalp are in children There are three general varieties of ringworm in this area, the most common one of which is illustrated by these cases The organism responsible for the disorder in this variety

is spoken of as the *Microsporon audouini*, and in fresh sodium or potassium hydroxid preparations, such as the one present under the microscope from one of these children, is seen the hair stump so thickly surrounded by small spores as to give it the appearance of a mosaic. About 95 per cent of the cases of ringworm of the scalp in this locality are of this type The disorder is highly infectious, as is illustrated by the fact that if one child of a family has it, usually several or all of them are affected There are few or no subjective symptoms, and the disorder disappears spontaneously, for some unknown reason, at the age of puberty

This type of ringworm begins as one or more patches in which the hairs appear to be nibbled off a few millimeters above the level of the scalp These patches gradually enlarge and fuse, not uncommonly to such an extent as to involve practically the entire scalp Ordinarily, however, there are present from three to a dozen such patches Many of the hair stumps have a whitish sheath about them, and the patch in general has the appearance of having been strewn with ashes, this grayish appearance being due to a fine scaling in the area There is usually no redness or other sign of inflammation of the underlying scalp here Permanent baldness does not result from this type of ringworm

The next most common type of ringworm of the scalp is called "kerion" and, unlike that just described, is moist Although it is seen most commonly in children it sometimes occurs in adults This variety is usually contracted from playing with animals that are infected with the causative organism, most commonly dogs and cats This variety constitutes only about 3 per cent of the cases of ringworm of the scalp Apparently it is not so infectious as the type previously described, but the infected child should not be allowed to attend school until he is pronounced non infectious by a physician This type usually occurs as from one to three or four swellings, varying in size from that of a hazelnut to that of a hen's egg The swellings are somewhat tender Not uncommonly the lymph glands of the neck are slightly enlarged The lesions of the scalp are soft and feel as though, upon puncture, pus would be evacuated, but they do not contain pus The hairs in the area are usually broken off

at various lengths, and the inflammation present pushes these hairs from their follicles in the course of a few days or weeks From the gaping follicle mouths a colorless, syrupy fluid exudes Any hairs in the area can be pulled out like pins from a pin-cushion After a variable period of time, usually several weeks, the disorder clears up spontaneously, but proper treatment hastens the disappearance of the lesions and prevents the spread of the infection to other parts of the scalp and to persons with whom the affected individual is associated Scarring, with baldness, usually results from this type of ringworm

The spread of the infection is prevented and the duration of the disorder is lessened if a 10 to 15 per cent sulphur or white precipitate ointment is used on the lesions morning and evening, and applied to the entire scalp once weekly

A third type of ringworm of the scalp, the rarest type, occurs as black dots, the size of a pin-head or smaller, scattered over the scalp Ordinarily, it can be detected only by the expert eye, although sometimes it is first noticed by the observant mother or attendant when she is shampooing the child's hair It causes very little loss of hair and is responsible for no irritation This type, like the first described, is of human origin The black dots mentioned may be seen even in individuals with light hair They are produced by the growth of a single hair curled upon itself beneath a small transparent scale No scarring results

So far as the treatment of the other first and last mentioned varieties is concerned, local treatment in the form of ointments and lotions is effective in something less than 50 per cent of the cases The ointments commonly used are strong salicylic acid preparations, such as the so-called "Whitfield ointment," which contains 6 per cent salicylic acid and 12 per cent benzoic acid in petrolatum, or an ointment containing 12 per cent of iodin crystals in goose grease, these preparations to be rubbed into the patches nightly

In case the individual does not respond satisfactorily to these or similar simple local measures, it may be necessary to produce complete epilation of the scalp either by means of the x-rays or by the ingestion of thallium acetate Neither one of

these measures is without danger, and they should not be resorted to if the child is near the age of puberty, in which case it is best that he be allowed to outgrow the disorder The dosage of thallium acetate must be measured extremely accurately, according to the weight of the individual It is given in a single dose by mouth The hair falls in between two and three weeks after the drug has been administered and begins to return in the course of about three months *x* Ray epilation of the scalp hair should be carried out only by one skilled in this procedure, by way of avoiding, to as great an extent as possible, the dangers which may arise from improper x ray technic

ALOPECIA AREATA

A boy aged eight years comes in because of complete absence of scalp hair of about one year's duration For two or three months previous to this there had been present several coin sized bald patches these gradually enlarging and fusing until all the scalp hair was gone The eyebrows and eyelashes are unaffected as is the lanugo hair of the body elsewhere His general health so far as the mother knows is good

Alopecia areata is a disorder of unknown origin which is responsible for loss of hair in patches It affects persons of all ages, but is more common in young people The patches vary in number from one to six or more and when first noticed are usually about the size of a finger nail They gradually enlarge and not uncommonly fuse to form large irregular areas Usually all the hair in the patches is absent, a white, shiny scalp being seen in these areas If the patches are spreading, numerous hair stumps about a quarter of an inch in length are seen at the edge These hairs are much wider and more heavily pigmented where they are broken off than where they enter the hair follicles This phenomenon gives them the appearance of exclamation points, and they are therefore called "exclamation point hairs" When the patches are no longer spreading, and the hair is growing again in the areas, the exclamation point hairs are not found There is almost never any redness, scaling, or other sign of inflammation, and there are no subjective symptoms Rarely is the hair of other areas affected notably the

bearded region, eyebrows, eyelashes, and armpits In rare instances the entire body becomes devoid of hair, and one sometimes sees total alopecia of the scalp in the absence of involvement elsewhere, such as in the patient here demonstrated The cases which present total alopecia are probably most common in children, and these are the most resistant to treatment

There is good evidence that the disorder is related in some way to the nervous system If the alopecia is total, it can frequently be demonstrated that there is some derangement of the glands of internal secretion or that congenital syphilis is a factor

As stated, the hair practically always comes back, the exception being the cases of total alopecia in children, and even in some of these instances the hair becomes entirely restored

Because of the numerous possibilities as to the causative factors in this disorder each case is an individual problem and can, therefore, be worked out only by painstaking efforts The local treatment consists in the use of stimulating ointments and lotions, and sometimes the irradiation of the scalp with ultraviolet rays The care of the individual's general health is of the utmost importance